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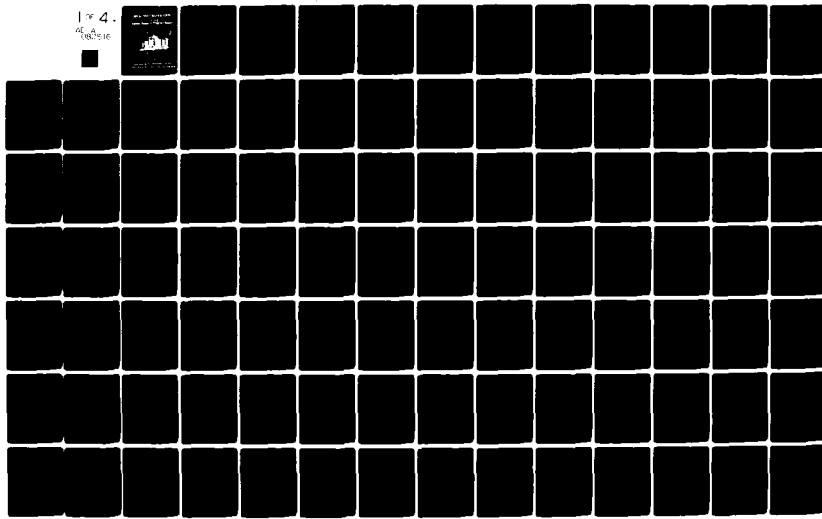
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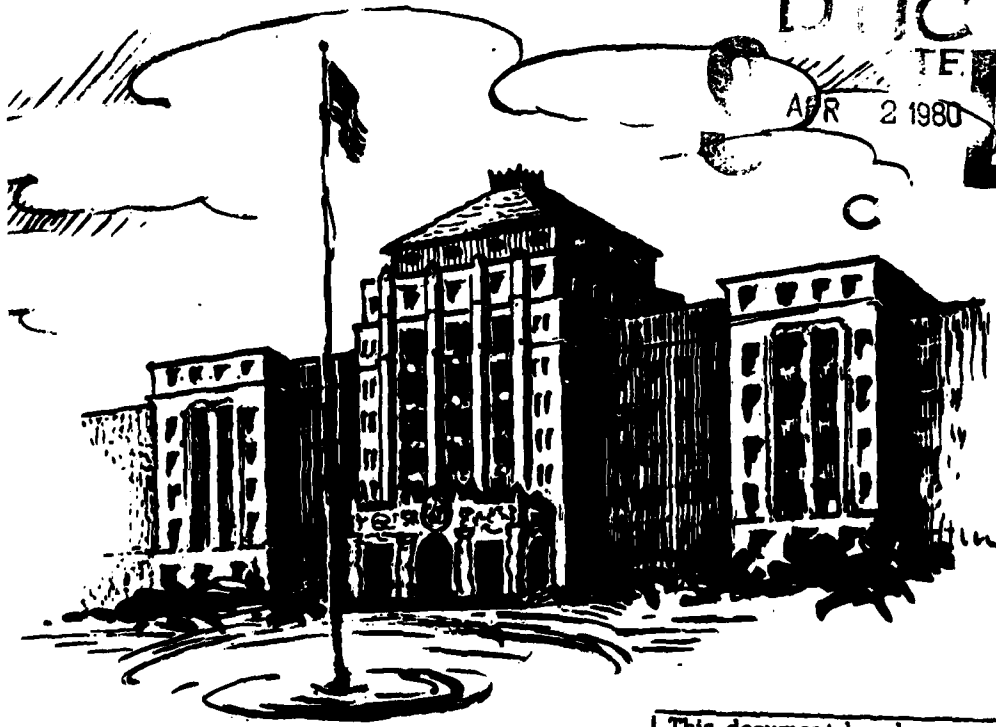
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CLINICAL INVESTIGATION SERVICE LEVEL Annual Research Progress Report

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FISCAL YEAR 1979

**Brooke Army Medical Center
Fort Sam Houston, Texas 78234**

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Subject report identifies the research activities conducted by Brooke Army Medical Center investigators through protocols approved by the Clinical In- vestigation Committee and the Human Use Committee for registrations with the Clinical Investigation Service during Fiscal Year 1979 and other known pre- sentations and publications by the Brooke Army Medical Center professional staff. A resume of each protocol giving the objectives, technical approach and progress is presented.		

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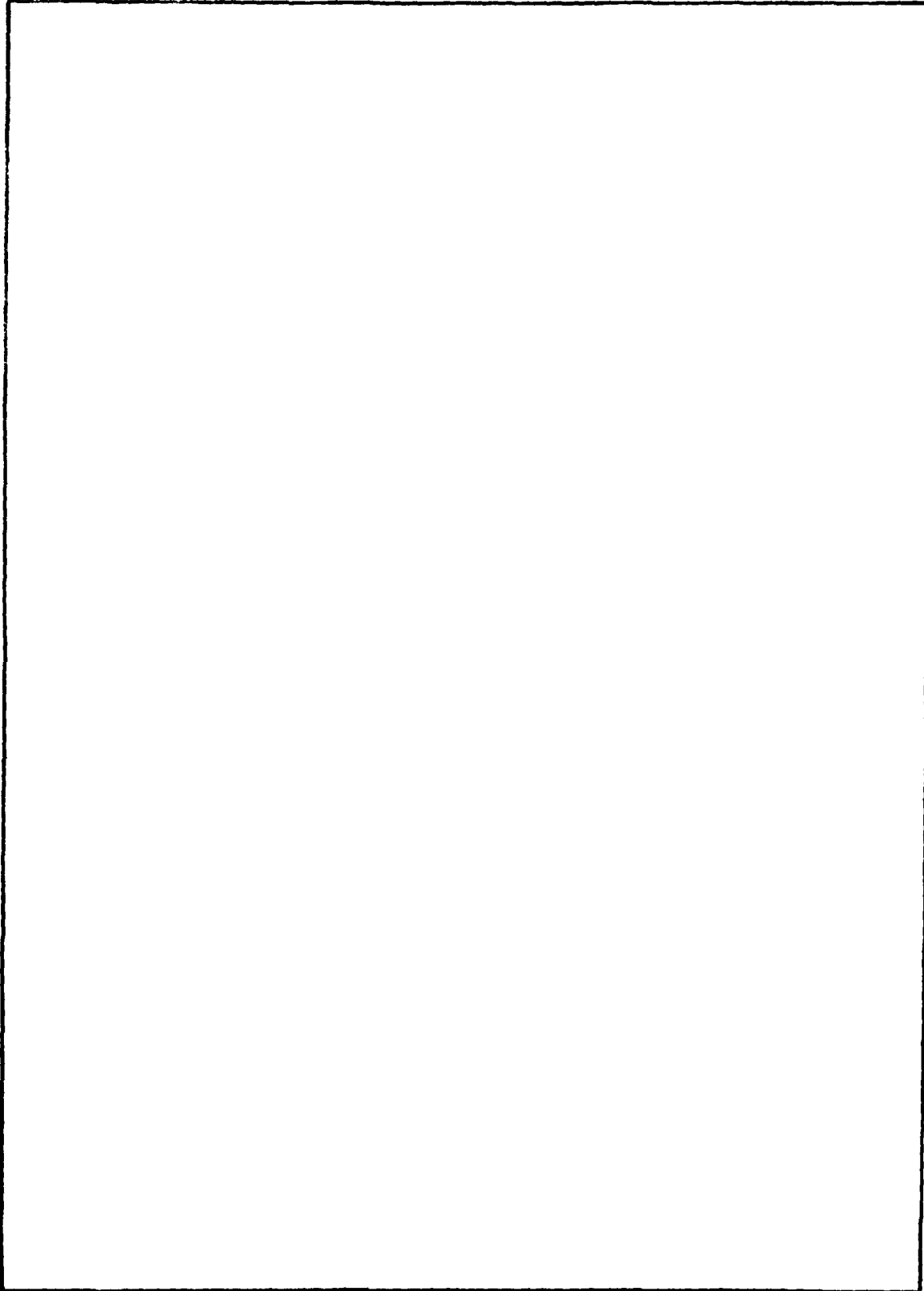
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FOREWORD

Our Clinical Investigation program has had a very successful year. Sheer numbers don't, obviously, tell the story but I think they give a rough idea of the work that is going on at Brooke Army Medical Center. During the past year, there were 108 publications in major medical journals, 97 presentations at national and international meetings, and 37 publications presently are "in press". Twenty-three protocols were completed during this fiscal year, 17 were terminated, 1 was transferred to another medical center and presently 56 are still active. Likewise, Brooke is active in several national protocol groups for the treatment of malignant disease: Southwest Oncology Group, Gynecology Oncology Group, and Polycythemia Vera Study Group. One hundred and nine protocols were being pursued during the past fiscal year, and 23 of these studies were completed. At present there are 86 protocols active.

The continued support of the BAMC Commander, his administrative staff, the professional medical staff, and the Clinical Investigation Committee has enabled this service to continue to perform high quality research. We have been very fortunate that our Commander, BG Andre J. Ognibene, feels that clinical investigation is important. His support has been most appreciated and has resulted in the success that the program presently enjoys.

Without the help of Mrs. Dodie Bratten, this annual report would not have been published in timely fashion; the service itself would not have run efficiently. Her work entails not only the day-to-day running of the Clinical Investigation Office, but includes her active participation in the Clinical Investigation Committee, Human Use Committee, and in all administrative committees associated with clinical investigation activity both here and at Health Services Command. This service to us is gratefully acknowledged.

We were disappointed that LTC Theodore R. McNitt left the Army and went into private practice. His contributions to the service during the first nine months of fiscal year 1979 were a main factor in the results that you will read.

Charles T. Thornevard

CHARLES T. THORNSVARD, M.D.
Lieutenant Colonel, MC
Acting Chief,
Clinical Investigation Service

REPORT OF TOTAL ACTIVITIES OF CLINICAL INVESTIGATION SERVICE

Fiscal Year 1979

A. Objectives

The Clinical Investigation Service was established at Brooke Army Medical Center 9 August 1971 to coordinate clinical investigation activities throughout the hospital complex. It is an independent service directly under the Chief, Professional Services and operated under the guidance of the Clinical Investigation Committee, composed of three members from the Department of Medicine; two from Department of Surgery; and one each from the Department of Obstetrics and Gynecology and Department of Pathology and ALS; and the Human Use Committee composed of lay personnel.

The Clinical Investigation Service was established to promote, stimulate, coordinate, and provide support for clinical investigation and development activities within Brooke Army Medical Center including design of experiments, typing and editorial services, and technical liaison with outside facilities.

B. Technical Approach

Manpower

<u>Name</u>	<u>Rank</u>	<u>Authorized</u>	<u>Title</u>
McNitt, Theodore R.	LTC		Acting Chief
Burleson, David G.	MAJ	68C00 8Z	Laboratory Dir/Biochemist
Lieberman, Michael	CPT	68J00 8Z	Microbiologist
Giolma, John P.	CPT	68Z00 8Z	Physiologist
Madonna, Gary S.	1LT	68A00 00	Microbiologist
Greene, Joseph C.*	SFC	92B3R	Sr Med Lab Sp, NCOIC
Loyd, Charles M.	SFC	92B3R	Sr Med Lab Sp, NCOIC
Sinegal, John H.	SSG	92B2R	Med Lab Sp
Hunter, Deborah	SP5	01H2R	Biological Science Asst
Wright, Gwendolyn	SP5	01H2R	Biological Science Asst
Ishibashi, Lillian	SP5	74F20N9	Programmer/Analyst
Kelly, Jack	SP4	92B10	Med Lab Sp
Wolcott, Karen	PFC	92B10	Med Lab Sp
Bagwell, James	GS11	00334	Computer Sp
Strong, GERALYN	GS7	00404	Biological Lab Tech
Chapa, Isidoro	GS7	00645	Med Lab Tech
Bratten, Dodie	GS7	01087	Editorial Asst

*NCOIC, October 1978-April 1979.

Clinical Investigation Committee

FY 79

<u>Name</u>	<u>Rank</u>	<u>Organization</u>	<u>Title</u>
McNitt, Theodore R.	LTC	Department of Medicine	Chairman
Burleson, David G.	CPT	Clinical Investigation Service	Recorder
Shock, John P.	COL	Department of Surgery	Member
Harris, Robert D.	CDR	Department of Surgery	Member
Leman, Milton H.	LTC	Department of Obstetrics and Gynecology	Member
Kies, Merrill S.	MAJ	Department of Medicine	Member
Humphrey, Stephen	MAJ	Department of Medicine	Member
Cerezo, Lizardo	MAJ	Department of Pathology and Area Lab Svcs	Member

FY 80

Thornsvar, Charles	LTC	Department of Medicine	Chairman
Burleson, David G.	MAJ	Clinical Investigation Service	Recorder
Harris, Robert D.	CDR	Department of Surgery	Member
Lowell, George G.	LTC	Department of Surgery	Member
Leman, Milton H.	LTC	Department of Obstetrics and Gynecology	Member
Kies, Merrill S.	MAJ	Department of Medicine	Member
Humphrey, Stephen	MAJ	Department of Medicine	Member
Cerezo, Lizardo	MAJ	Department of Pathology and Area Lab Svcs	Member

Funding FY 79

MEDCASE	\$ 99,684.39	1 Protocol
	\$ 4,330.00	Laboratory
	<u>\$104,014.39</u>	
Capital Equipment	\$ 3,000.00	Laboratory
Consumable Supplies	\$ 19,636.65	10 Protocols
	\$ 27,029.43	Laboratory
	<u>\$ 1,226.55</u>	Contractual Services
	\$ 47,892.63	
TOTAL	\$154,907.02	

C. Progress

Protocol Disposition FY 79

	<u>Completed</u>	<u>Terminated</u>	<u>Transferred</u>	<u>Ongoing to FY 80</u>
FY 73	-	-	-	1
FY 74	-	-	-	1
FY 75	-	-	-	2
FY 76	1	2	-	1
FY 77	3	4	-	10
FY 78	15	6	-	13
FY 79	<u>4</u>	<u>5</u>	<u>1</u>	<u>28</u>
	23	17	1	56

Twenty-three Southwest Oncology Group protocols were completed during FY 79. Group protocols ongoing to FY 80 are as follows: Polycythemia Vera Study Group - 9; Gynecology Oncology Group - 21; Southwest Oncology Group - 56.

During FY 79, 108 manuscripts were accepted for publication in national and international journals. At the present time there are 37 manuscripts pending acceptance for publication. Thirty-four manuscripts were reviewed for fulfillment of residency training requirement. Ninety-seven presentations were made at national and international meetings with much of the material emanating from Clinical Investigation Service sponsored projects.

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Code:

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* - Clinical
+ - Chronological Order of Registration
- - Fiscal Year in Which Registered

C - Completed
O - Ongoing
T - Terminated
TR - Transferred

P - Published
SP - Submitted for Publication
PR - Presentation

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CLINICAL INVESTIGATION SERVICE

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Lieberman, M.M. Characterization of Pseudomonas ribosomal vaccine by density gradient centrifugation. Poster presentation at annual meeting of the American Society for Microbiology, 4-8 May 1979, Los Angeles, Calif.

Lieberman, M.M. Research on Pseudomonas ribosomal vaccines. Presented to Pseudomonas Society, American Society for Microbiology, 6 May 1979, Los Angeles, Calif.

Allen, R.C. The role of O_2 in phagocytosis and microbicidal action of polymorphonuclear leukocytes: An approach employing chemiluminescence. 7th annual meeting of the American Society of Photobiology, 24-28 June 1979, Monterrey, Calif.

Allen, R.C. Chemiluminescence: An approach to the study of the humoral-phagocyte axis in host defense against infection. International Conference on Liquid Scintillation Applications and Development, 20-24 August 1979, San Francisco, Calif.

Giolma, J.P. Pulmonary artery input impedance measurements in man. 51st Scientific Sessions of the American Heart Association, 13-16 November 1978, Dallas, Texas.

Department of Medicine

Slay, L. Use of triage system in an APC system. Fourth Conference on Ambulatory Patient Care, 29-30 August 1979, Fort Sam Houston, Texas.

Slay, L. Using research to lower ambulatory patient care costs. Fourth Conference on Ambulatory Patient Care, 29-30 August 1979, Fort Sam Houston, Texas.

Slay, L. The effect of audit on AMOSIST performance. Fourth Conference on Ambulatory Patient Care, 29-30 August 1979, Fort Sam Houston, Texas.

Slay, L. L.E., Cecere, F.A., VanCleave, S. Ambulatory care audit in a teaching hospital. Fourth Conference on Ambulatory Patient Care, 29-30 August 1979, Fort Sam Houston, Texas.

Slay, L.E., Wolcott, B.W. A detailed time study in a "walk-in" clinic. Fourth Conference on Ambulatory Care, 29-30 August 1979, Fort Sam Houston, Texas.

Allergy-Immunology

Huss, R.W. A comparative efficacy study of nebulized albuterol vs. isoproterenol in the treatment of asthma. November 1978, Denver, Colo.

Laham, M.N. Allen, R.C., Greene, J.C. Allergic bronchopulmonary aspergillosis (ABPA) caused by Aspergillus terreus: Specific lymphocyte sensitization and antigen-directed serum opsonic activity. American Academy of Allergy, 25-29 March 1979, New Orleans, La.

Cardiology

Murgo, J.P. Manipulation of aortic pressure and flow wave reflections with the Valsalva maneuver. 51st Scientific Sessions of the American Heart Association, 13-16 November 1978, Dallas, Texas.

Murgo, J.P. Aortic valve gradients in normal man during exercise and isoproterenol infusion - relationship to pulsatile flow. 51st Scientific Sessions of the American Heart Association, 13-16 November 1978, Dallas, Texas.

Uhl, G.S. Ventricular volume dependent changes in electromechanical delay. 51st Scientific Sessions of the American Heart Association, 13-16 November 1979, Dallas, Texas.

Murgo, J.P. Ascending aorta pressure waveshape - relationship to input impedance. 51st Scientific Sessions of the American Heart Association, 13-16 November 1978, Dallas, Texas.

Bowers, R.E. Exercise induced changes in splitting of the second heart sound in normal man. 51st Scientific Sessions of the American Heart Association, 13-16 November 1978, Dallas, Texas.

Murgo, J.P. Chairman session on Clinical Research - Laennec Society, 51st Scientific Sessions of the American Heart Association, 13-16 November 1978, Dallas, Texas.

Murgo, J.P. Panel member, 28th Annual Sessions of the American College of Cardiology. Physiologic Basis of heart sounds and murmurs. March 1979, Miami, Florida.

Murgo, J.P. Hemodynamic profile of the cardiomyopathies. Presbyterian Hospital and University of Texas Health Science Center, April 1979, Dallas, Texas.

Murgo, J.P. Hemodynamics of pericardial tamponade. Presbyterian Hospital and University of Texas Health Science Center, April 1979, Dallas, Texas.

Murgo, J.P. Research seminar series - Injection dynamics in obstructive and nonobstructive hypertrophic cardiomyopathy. University of Texas Health Science Center at San Antonio, June 1979.

Murgo, J.P. Hemodynamic profile of the cardiomyopathies. University of Texas Health Science Center at San Antonio, September 1979.

Craig, W.C. Aortic valve gradients induced by isoproterenol infusion in normal and hypertrophic cardiomyopathy patients. Army Association of Cardiology, Madigan Army Medical Center, May 1979, Tacoma, Wash.

Davis, R.C. Exercise induced changes in splitting of the second heart sound in normal man. Army Association of Cardiology, Madigan Army Medical Center, May 1979, Tacoma, Wash.

Bloom, K.R. Myocardial function in thalassemia major: An echocardiographic study. Army Association of Cardiology, Madigan Army Medical Center, May 1979, Tacoma, Wash.

Humphrey, S.H. Hemoglobin oxygen carrying capacity during sodium nitroprusside infusion. Society of Critical Care Medicine, 28-30 May 1979, San Francisco, Calif.

Dermatology

Rietschel, R.L. A method to evaluate skin moisturizers in vivo. Society of Cosmetic Chemists, 3 May 1979, Dallas, Texas.

Rietschel, R.L. Minocycline and the black thyroid gland. South Central Dermatologic Congress, 27 January 1979, Houston, Texas.

Fulkerson, A.R. Minocycline and the black thyroid gland. American College of Physicians, 25 March 1979, San Francisco, Calif.

Jucas, J.J. Bullous mycosis fungoides. American Academy of Dermatology, 3 December 1978, San Francisco, Calif.

Hudson, L.D. Erythema annulare centrifugum. American Academy of Dermatology, December 1978, San Francisco, Calif.

Emergency Medicine

Szalanski, J.J.J., Bushyhead, J.B. Physicians' neglect of pertinent negatives that predict the presence of pneumonia. American Federation for Clinical Research, 9 February 1979, Carmel, Calif.

McNitt, H. Computer-based audit and research in the ED. American Society of Emergency Physicians, 23-26 May 1979, Miami, Florida.

Wolcott, B.W. A Venn diagram to assist in house staff education. American Society of Emergency Physicians, 23-26 May 1979, Miami, Florida.

Ognibene, M. The time relationship of performance and audit feedback on conformance with ED process criteria. American Society of Emergency Physicians, 23-26 May 1979, Miami, Florida.

Vaughn, P.B. Effective algorithm-based triage and self-care protocols: quality medicine at lower costs. American Society of Emergency Physicians, 23-26 May 1979, Miami, Florida.

Hematology

Rubin, R.N. Coagulation testing in cancer patients. Temple University Hospital, 17 October 1978, Philadelphia PA.

Rubin, R.N. Studies on march hemoglobinuria. American College of Physicians, 10-14 March 1979, San Antonio, Texas.

Nephrology

Ulrych, M. Is the decrease in vascular capacitance (VC) rather than volume overload the major hemodynamic mechanism in essential hypertension (EH)? International Society of Hypertension, June 1979, Stockholm, Sweden.

Oncology

McCracken, J.D. Combination chemotherapy, radiotherapy, and immunotherapy for oat cell carcinoma of the lung. XII International Cancer Congress, 5-11 October 1978, Buenos Aires, Argentina.

Department of Pathology and ALS

Head, D.R. Enlisted technologist training. Current Concepts in Pathology, Walter Reed Army Medical Center, 23-25 April 1979.

Head, D.R. Classification of lymphomas. Panamanian Pathology Society, 16 July 1979, Panama Canal Zone.

Head, D.R. Hemoglobinopathies. Coco Solo Hospital, 17 July 1979, Panama Canal Zone.

Head, D.R. Leukemia classification and special stains. Isthmian Medical Society, 17 July 1979, Panama Canal Zone.

Jereb, J.A. Hemoglobinopathies and thalassemia. 20-25 May 1979, Mayo Clinic, Rochester, Minn.

Jereb, J.A. The diagnosis and classification of the acute leukemias. Colorado Association for Continuing Medical Laboratory Education, 6 August 1979, Colorado Springs, Colo.

Department of Pediatrics

Wilson, F.P. Algorithm-directed triage - A prospective study. Fourth Conference on Ambulatory Patient Care, 29-30 August 1979, Fort Sam Houston, Texas.

Wilson, L.O. Pediatric AMOSISTS: The pilot project. Fourth Conference on Ambulatory Patient Care, 29-30 August 1979, Fort Sam Houston, Texas.

Department of Psychiatry

Worthington, E.R. Role of the division psychologist in combat. Current Trends in AMEDD Psychology, William Beaumont Army Medical Center, November 1978, El Paso, Texas.

Worthington, E.R. Status of AMEDD psychologists in the 1979's. Current Trends in AMEDD Psychology, William Beaumont Army Medical Center, November 1978, El Paso, Texas.

Worthington, E.R. Economics of Human Resources in the U.S. Army. Regional Conference of the Inter-University Seminar on Armed Forces and Society, U. S. Naval Post-Graduate School, May 1979.

Worthington, E.R. Psychological adjustment of repatriated Vietnam POWs. American Psychological Association Conference, September 1979, New York, City.

Worthington, E.R. Stress management. National Association of Executive Secretaries Conference, September 1979, Las Vegas, Nev.

Department of Radiology

Sorgen, S.D. Concurrent hydroxyurea and bleomycin with full course radiotherapy in the treatment of advanced head and neck cancers. 20th Annual Meeting, American Society of Therapeutic Radiologists, 31 October 1978, Los Angeles, Calif.

Department of Surgery

Anesthesiology

Anderton, B. Human placental passage of Naloxone. Society for Obstetrical Anesthesia and Perinatology, November 1978, Winston Salem, N.C.

Pace, N.L., Parrish, R.G., Lieberman, M.M. Halothane anesthesia and narcotic antagonists in the dog.

Cardiothoracic Surgery

Oddi, M.A. Constrictive pericarditis following coronary artery bypass surgery. Association of Army Cardiology, Madigan Army Medical Center, 17-19 May 1979, Tacoma, Wash.

General Surgery

Young, R.N. Surgical correction of hypoglycemia in infancy. South Texas Chapter, American College of Surgeons, 9 February 1979.

Reed, K. Pancreatic carcinoma: thirty years experience. Southwestern Surgical Congress, 26 April 1979.

Young, R.N. Tetanus revisited and updated. Southwestern Surgical Congress, 26 April 1979.

Piskun, M.A. Pancreatic pseudocyst. Gary Wratten Symposium, 18 May 1979.

Bowman, G. Chronic pancreatitis: Evaluation and diagnosis. Gary Wratten Symposium, 18 May 1979.

Jarstfer, B.S. Non-invasive diagnosis in cerebrovascular disease. Gorgas Hospital, Canal Zone, 30 May 1979.

Jarstfer, B.S. Renovascular hypertension. Gorgas Hospital, Canal Zone, 29 May 1979.

Jarstfer, B.S. Risk factors in atherogenesis. Gorgas Hospital, Canal Zone, 29 May 1979.

Jarstfer, B.S. The reflected wave in vascular diagnosis. Military Vascular Symposium, 14 December 1978.

McGrath, R.S. The reflected wave study. 2nd Annual Scientific Meeting Society of Non-Invasive Vascular Technology, 26-27 June 1979, Nashville, Tenn.

Neurological Surgery

Harris, R.D. Neurovascular compression of the ventrolateral medulla - theoretical considerations and experimental model. Congress of Neurological Surgeons, 7-19 October, Las Vegas, Nev.

Harris, R.D. Inappropriate secretion of vasopressin - experimental model. Society of Neurological Surgeons, May 1979, Greenbriar, West Virginia.

Harris, R.D. Spinal cord compression and vasopressin - experimental model. Society of Neurological Surgeons, May 1979, Greenbriar, West Virginia.

Orthopaedics

McIlwain, W. Treatment of Legg-Calve-Perthes disease. Society of Military Orthopaedic Surgeons, 12-16 November 1978, Naval Regional Medical Center, Portsmouth, Va.

Peters, V. Operative reduction and internal fixation technique for fractures of the foot. U.S. Air Force Podiatry Seminar, February 1979, Brooks Air Force Base, Texas.

Peters, V. Treatment of trauma to the foot and ankle. Texas State and Tri-State Podiatry Seminar, 24-26 May 1979, Houston, Texas.

Peters, V. Primary malignancies of the foot, El Paso Texas Medical Society, 15 June 1979, El Paso, Texas.

Peters, V. Guest Lecturer. 33rd Southwestern Podiatry Congress, 6-8 June 1979, Houston, Texas.

Otolaryngology

Price, J.C. A sublabial approach to the nasal and nasopharyngeal cavities. The Society of Head and Neck Surgeons, April 1979, Pittsburgh, Pa.

Price, J.C. Hyperbaric oxygen in the treatment of rhinocerebral mucormycosis. The Triologic Society, April 1979, Los Angeles, Calif.

Tretta, J. Combined surgical management of a juvenile nasopharyngeal angiofibroma: A case report. 63rd Annual Clinical Assembly The Osteopathic College of Ophthalmology and Otolaryngology, May 1979, Sulphur Springs, West Virginia.

Ritter, R. Audiology management information system. American Speech and Hearing Association, 18-21 November 1978, San Francisco, Calif.

Ritter, R. The controversial loudness discomfort level-acoustic reflex threshold relationship. American Speech and Hearing Association, 18-21 November 1978, San Francisco, Calif.

Ophthalmology

Main, C.E. Relative afferent pupillary defects in association with optic tract lesions. Bascom Palmer Eye Institute Resident's Day, 7-10 June 1979, Miami Beach, Florida.

Urology

Gangai, M.P. Pediatric abdominal masses. Central Texas Association of Military Physicians Assistants, 26-28 October 1978, San Antonio, Texas.

Spence, C.R. Congenital hydronephrosis of the lower pole in a duplex kidney. Kimbrough Urological Seminar, 12-18 November 1978, San Antonio, Texas.

Solomon, H.D. Ureteral triplication: An unreported variant. Kimbrough Urological Seminar, 12-18 November 1978, San Antonio, Texas.

Gangai, M.P. Primary transitional cell carcinoma of the ureter. Kimbrough Urological Seminar, 12-18 November 1978, San Antonio, Texas.

Gangai, M.P. Pediatric abdominal masses. Focus on Urology Update 79. American Urological Association Allied, Southern California Chapter, February 1979, Los Angeles, Calif.

Gangai, M.P. Primary transitional cell carcinoma. Western Section AUA, March 1979, Tucson, Ariz.

Gangai, M.P. The clinical significance of hematuria. American Urological Association Allied, Phoenix Chapter, March 1979.

Gangai, M.P. Urethral stricture disease in the male. American Urological Association Allied, Phoenix Chapter, March 1979.

Spence, C.R. Prevention of failures of varicocele surgery. Western Section, American Urological Association, March 1979, Tucson, Ariz.

Gangai, M.P. Patch graft urethroplasty. American College of Surgeons, April 1979, Denver, Colo.

Gangai, M.P. The use of full thickness free skin grafts in the treatment of urethral strictures in the male. Movie shown at the Western Section AUA, March 1979, Tucson, Ariz., and American College of Surgeons meeting, April 1979, Denver, Colo.

Oral Surgery Service

Shelton, D.W. Techniques in outpatient general anesthesia. American Association of Oral and Maxillofacial Surgeons, 14-18 September 1979, New Orleans, La.

Physical Therapy Service

Osburn, M.S. Early intervention program for high risk infants. Scientific exhibit, American Physical Therapy Association Convention, 10-15 June 1979, Atlanta, Georgia.

Social Work Service

Worline, M. Workshop on "Battered Wives". National Association of
Christians in Social Work, 28-30 March 1979, Columbus, Ohio.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

MANUSCRIPTS SUBMITTED FOR PUBLICATION

Department of Medicine

Blanck, R.R., Ream, N.W., Deleese, J.S. Medical complications of illicit drug use. Medicine.

Allergy-Immunology

Laham, M.N., Panush, R.S., Caldwell, J.R. Modulation of lymphocyte proliferative responses to mitogens and antigens by complement components C₁, C₄ and C₂. Journal of Clinical Investigation.

Dermatology

Williams, L.R., Rietschel. Pustular ioderma complicating cardiovascular surgery. Annals of Thoracic Surgery.

Fulkerson, A.R., Rietschel, R.L., Thomason, A.M., Johnson, R.G. Minocycline induced thyroid gland pigmentation and dysfunction. Journal of the American Academy of Dermatology.

Williams, L.R. Gold dermatitis. Journal of the Association of Military Dermatologists.

Beachler, K.J. Perioral dermatitis - a review. Journal of the Association of Military Dermatologists.

Rietschel, R.L., Jucas, J.J., Lewis, C.W. Connubial contact dermatitis to glycerin and mineral oil. Archives of Dermatology.

Hudson, L.D. Babcock, W.S. Multiple persistent histiocytomas. Journal of the American Academy of Dermatology.

Emergency Medicine

Grossling, S.F. Primary lymphosarcomas of the gastrointestinal tract. Annals of Surgery.

Wolcott, B.W. The physician interest quotient: A vital sign at initial patient contact. JACEP.

Wolcott, B.W., Brugger, A.M., Wood, R.W. Management of blunt extremity trauma by algorithm-directed military corpsmen. Journal of the American Medical Association.

Endocrinology

Thomason, A.M. Combination of carotid body tumors and pheochromocytomas in two sisters. Science.

Gastroenterology

Chernoff, R., Dean, J.A. Medical and nutritional aspects of intractable diarrhea. Journal of the American Dietetic Association.

O'Meara, T.F. Gastrointestinal polyposis syndromes. Journal of Digestive Diseases.

Infectious Disease

Potts, D.W. Disseminated Neisseria gonorrhoeae. British Journal of Venereal Diseases.

Nephrology

Wright, L.F. The role of renal biopsy in clinical practice. Annals of Internal Medicine.

Neurology

Polsky, M.M. Bio-Logic, Bio-Mathematic, and Physiologic Principles of Mind. Publisher undetermined.

Joyce, R.P., Gunderson, C.H. Carbamazepine (Tegretol) induced orofacial dyskinesia. Annals of Neurology.

Oncology

McCracken, J.D. et al. 5-Fluorouracil, Methyl CCNU and Radiotherapy with or without Testolactone for localized adenocarcinoma of the exocrine pancreas. Journal of Cancer.

Cowan, J.D., Rubin, R.N., Kies, M.S., Cerezo, L. Bone marrow necrosis. Cancer.

Kies, M.S., Abbott, O.D., Rubin, R.N. Recurrence of hemolysis in hereditary spherocytosis: A case due to leukemic infiltration of an accessory spleen. American Journal of Medicine.

Department of Nursing

Molter, N.C. The shock syndrome, part I and part II. Journal of Nursing.

Department of Pathology and ALS

Mendoza, A. Primary canine cutaneous meningioma. A light and electron microscopic study. *Veterinary Pathology*.

Dunn, B.C. Hemolytic disease of the newborn caused by anti-Go^a. *Transfusion*.

Seal, L.A., Jamison, R.M. Oxauracil typing of Herpesvirus simplex type I and II. *Journal of Medical Virology*.

Seal, L.A., Jamison, R.M. Evaluation of the effectiveness of 2H-1, 3-Oxazine-2, 6(3H) - dione (Oxauracil) in the treatment of Herpesvirus simplex (HSV) induced acute encephalitis in mice. *Antimicrobial Agents and Chemotherapy*.

Department of Pediatrics

Wilson, L.O., Wilson, F.P., Canales, L. Algorithm-directed triage in pediatrics: A safe system that facilitates the study and planning of nonappointed health care. *Journal of the American Medical Association*.

Wheeler, M., Wilson, F.P., Wilson, L.O. Algorithm-directed care by physician extenders in a pediatric population - part I. *Pediatrics*.

Wilson, L.O., Wilson, F.P., Ratner, P.H. Children of the night. *JACEP*.

Department of Radiology

Wymer, David C. Simulation of bilateral adrenal uptake of ^{99m}Tc di-phosphonate following radiotherapy. *American Journal of Roentgenology*.

Hill, M.E. Ultrasound in the evanescent abdominal mass: A case report. *Journal of Clinical Ultrasound*.

Department of Surgery

Anesthesiology

Scavone, J.A. An unusual cause of complete upper airway obstruction on induction of general anesthesia. *Anesthesia and Analgesia*.

Cardiothoracic Surgery

Oddi, M.A. et al. Postoperative total pulmonary torsion. *Annals of Thoracic Surgery*.

General Surgery

Deal, V.T. et al. Leiomyoblastoma in a twelve-year-old girl. *Pediatrics*.

Orthopaedics

Parr, T.J. Nonorbital osteosarcoma following retinoblastom: A case report and review of the literature. Journal of Bone and Joint Surgery.

Otolaryngology

Tretta J.T. Combined surgical management of a juvenile nasopharyngeal angiofibroma: A case report. The Laryngoscope.

Perry, F.P. Hyperbaric oxygen in the treatment of rhinocerebral mucormycosis. The Laryngoscope.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of the Molecular Conformation of Erythromycin
2'Esters and Bioactivity.

WORK UNIT NO.: C-34-76

PRINCIPAL INVESTIGATORS: Dennis L. Stevens, M.D., MAJ, MC;
Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the nuclear magnetic resonance of various erythromycin 2'esters in order to predict the feasibility of developing better drugs for clinical use.

TECHNICAL APPROACH

Erythromycin is administered as the ester of a variety of fatty acids covalently bound to the 2' position. The biological activity and toxicity of these esters has been established; however, the subtlety of the substitutions does not suggest the wide range of response obtained from administering the different esters.

Nuclear magnetic resonance techniques will be used to determine the conformation of several esters of erythromycin as a function of pH. Specifically, we will measure the Spin Lattice relaxation times (T_1 's) of different functional groups in the molecule. We will correlate the conformational changes with intestinal absorption, antibiotic potency, and hepatic toxicity reported in the literature. Ideally, the in vitro data we collect, coupled with the physiological data found in the literature will enable us to choose an ester which will yield an intermediate conformational change and will retain the qualities necessary for effective clinical use.

Personnel: None

Funding: None

C-34-76 (Continued)

PROGRESS

Southwest Research Foundation was unable to furnish the personnel to perform the analysis of the erythromycin compounds by nuclear magnetic resonance. Therefore, the study was terminated.

Status: Terminated.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Development of a Gram-Negative Bacterial Vaccine for Laboratory Animals.

WORK UNIT NO.: C-7-77

PRINCIPAL INVESTIGATOR: Michael M. Lieberman, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: Gwendolyn Wright, SP5; Karen Wolcott, PFC

OBJECTIVES

To develop a safe and effective, broad-spectrum, gram-negative bacterial vaccine for laboratory animals.

TECHNICAL APPROACH

The initial phase of the project encompasses the development of a ribosomal vaccine for several serotypes of Pseudomonas aeruginosa. The bacteria are grown in broth culture, harvested and washed by centrifugation, and subjected to ultrasonic disruption for preparation of crude extracts. The ribosomes are isolated from the extracts by ammonium sulfate fractionation and ultracentrifugation. The isolated ribosomes are chemically analyzed for protein and RNA content and tested for immunogenicity in mice. Mice are given two vaccinations seven days apart and directly challenged by inoculation of live virulent organisms ten days after the second vaccination. Control (non-vaccinated) mice are also challenged. The percentage of mice that survive 48 hours post challenge are scored to determine the extent of protection afforded by the vaccine.

In addition, the vaccine is used to immunize rabbits and the rabbits bled to obtain immune serum. The immune serum is then tested by injecting it into mice which are subsequently challenged by inoculation with live bacteria. Mice that are injected with pre-immune rabbit serum are also included in the challenge as controls. The challenged mice are then scored for survival as above in order to determine the ability of the immune serum to confer passive protection against Pseudomonas to the mice.

Personnel: 1 SP5 (12 months)
1 SP5 (6 months)
1 PFC (6 months)

C-7-77 (Continued)

<u>Funding:</u>	FY 79	FY 78
Capital Equipment		\$1,214.00
Consumable Supplies	\$3,900.00	\$3,557.70

PROGRESS

Research performed prior to FY 79 has shown that ribosomal vaccines from Pseudomonas aeruginosa induced active immunity in mice and could raise specific antibody in rabbits capable of passive transfer of protection. The vaccine could be separated by gel filtration into two components, both of which were capable of inducing active immunity and producing protective antisera. The large component (Peak A) contained lipopolysaccharide in addition to ribosomal material, but the smaller component (Peak B), corresponding to 70S ribosomes, was free of detectable amounts of lipopolysaccharide. The relative importance of the IgG and IgM classes of antibodies was also compared. The results indicated that both IgG and IgM isolated from immune rabbit serum are protective in mice. Only IgG precipitated with the vaccine in AGD, but both IgG and IgM were active in PHA and in CF. The PHA titer of the IgM was higher than that of the IgG, but the CF titer of the IgG was higher than that of the IgM. The mouse protective capability of the IgG and IgM was about the same.

Research performed during FY 79 has characterized the vaccine by ultracentrifugation in sucrose density gradients after dissociation into ribosomal subunits by dialysis against buffer containing 10^{-3} or 10^{-4} m Mg^{++} . The isolated 50S and 30S subunit recovered from the gradients were subjected to serological analysis using a quantitative micro-complement fixation (CF) test. It was, therefore, concluded that (1) 60S ribosomes from a Pseudomonas ribosomal vaccine (the smaller component of the vaccine separated by gel filtration) can be dissociated into 50S and 30S subunits; (2) both isolated 50S and 30S subunits contain antigenic material, but the 30S subunit is more antigenic than the 50S subunit as determined by complement. Both subunits are capable of eliciting protective antibody in rabbits (although immunization in the presence of an adjuvant is required). (3) 30S ribosomal subunits which have been spontaneously degraded to smaller particles (about 22S) still retain their antigenic activity, and thus have higher complement fixing activity per OD₂₆₀ unit than 30S particles. (4) The larger component of the vaccine separated by gel filtration cannot be dissociated into ribosomal subunits by dialysis against buffer containing 10^{-3} or 10^{-4} m Mg^{++} , even though it has previously been shown to contain ribosomal material.

In addition, the antisera to these subcellular (ribosomal) vaccines has been shown to react with a surface component of whole bacterial cells, using a method involving polymorphonuclear leukocyte (PMN) chemiluminescence. In this technique (described elsewhere in the annual report

C-7-77 (Continued)

in detail), bacteria are opsonized by reaction with specific immune serum (antiserum to a ribosomal vaccine) and then undergo phagocytosis by the PMNL's which is accompanied by the emission of detectable light (chemiluminescence) from the PMNL's. This demonstration of opsonic activity by the antisera in vitro provides a functional basis for the protective activity of the antisera observed in vivo.

Status: Ongoing.

Lieberman, M.M., McKissock, D.C., and Wright, G.L. Passive immunization against Pseudomonas with a ribosomal vaccine-induced immune serum and immunoglobulin fraction. Infect Immun 23:507-521, 1979.

Lieberman, M.M., McKissock, D.C., and Wright, G.L. Characterization of Pseudomonas ribosomal vaccine by density gradient centrifugation. Poster presentation at annual meeting of the American Society for Microbiology, 4-8 May 1979, Los Angeles, California.

Lieberman, M.M. Research on Pseudomonas ribosomal vaccines. Presented to Pseudomonas Society, American Society for Microbiology, 6 May 1979, Los Angeles, California.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: In Vitro Studies of Amphotericin B.

WORK UNIT NO.: C-16-78

PRINCIPAL INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Dennis L. Stevens, M.D., Ph.D., LTC, MC; Michael M. Lieberman, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: Geralyn Strong, DAC

OBJECTIVES

To study the mechanism of polyene antibiotic action and to develop in vitro biological and physical techniques that will be useful in determining species specific efficacy and concentrations of selected polyene antibiotics.

TECHNICAL APPROACH

The two aspects of this protocol are 1) development of an electron spin resonance assay technique for Amphotericin B and 2) studies of factors affecting the in vitro efficacy of Amphotericin B.

Personnel: None

Funding: None

PROGRESS

Since it was not possible to develop an electron spin resonance assay technique for Amphotericin B, it was elected to terminate the study.

Status: Terminated.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Determination of Opsonizing Antibody in People Receiving Polyvalent Pneumococcal Vaccine.

WORK UNIT NO.: C-25-78

PRINCIPAL INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Robert C. Allen, M.D., Ph.D., CPT, MC

ASSOCIATE INVESTIGATORS: Dennis L. Stevens, M.D., LTC, MC; David W. Potts, M.D., MAJ, USAF MC.

OBJECTIVES

To determine the serum opsonizing activity in selected patients in response to a polyvalent pneumococcal vaccine.

TECHNICAL APPROACH

Pre-and post-immunization serum specimens were obtained from patients undergoing immunization against Streptococcus pneumoniae using a polyvalent vaccine. The activity of these sera relative to opsonification Streptococcus pneumoniae of different serotypes will be quantified by a new, highly sensitive chemiluminescent assay.

Personnel: None

Funding: None

PROGRESS

The sera to be studied has been collected, catalogued and stored at -70°C. The new method for quantifying anti-pneumococcal opsins is near completion. Data on effectiveness of the vaccination should be forthcoming.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Molecular Pathology of Alpha Toxin from Clostridium Perfringens
upon Polymorphonuclear Leukocyte (PMNL) Function.

WORK UNIT NO.: C-35-78

PRINCIPAL INVESTIGATORS: Dennis L. Stevens, M.D., Ph.D., LTC, MC;
Robert C. Allen, M.D., Ph.D., CPT, MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Michael M.
Lieberman, Ph.D., CPT, MSC; John H. Sinegal,
SSG; GERALYN Strong, DAC; John Posch, DAC;
Deborah Hunter, SP 5

OBJECTIVES

To study membrane alterations of PMNL resulting from the action of α -toxin
C. perfringens, the etiologic agent of gas gangrene.

TECHNICAL APPROACH

The purification of phospholipase C, the alpha toxin of C. perfringens,
was accomplished by column and electrophoretic technique. The action
of the isolated components with respect to PMN leukocyte activation was
studied using isotopic technique for measurement of carbohydrate meta-
bolism and chemiluminescence for assessment of oxidative activity.

Personnel: 1 GS-7 (3 months)
1 SSG (8 months)
1 SP5 (6 months)

<u>Funding:</u>	FY 79	FY 78
Consumable Supplies	\$5,236.25	\$ 790.93

PROGRESS

Alpha toxin has been found to activate the membrane of PMN leukocytes
as measured by the resulting oxidative activity. However, the enzy-
matic nature of this activation is complex and requires further

C-35-78 (Continued)

investigation. Activation does not appear to be exclusively associated with phospholipase C. The activation of PMN leukocytes by these toxins appears to metabolically stress the cells resulting in diminished microbicidal effectiveness.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Assessment of Opsonic Capacity and Phagocyte Functionality in
Microliter Quantities of Whole Blood.

WORK UNIT NO.: C-5-79

PRINCIPAL INVESTIGATOR: Robert C. Allen, M.D., Ph.D., CPT, MC

ASSOCIATE INVESTIGATORS: Geralyn Strong, DAC; Jack Kelly, SP4

OBJECTIVES

To research and develop a rapid, objective, and quantitative approach to the assessment of phagocyte activity in microliter quantities of whole blood by introduction of high quantum yield oxidizable substrate and use of photomultiplication techniques to quantitate chemiluminescence (luminescence resulting from chemical reaction).

TECHNICAL APPROACH

The role of specific antibody (IgG, IgM) classical pathway activation of complement, and alternative pathway activation of complement in the opsonification of bacteria and fungi, is presently under investigation. Opsonification is the process of immune recognition of an antigen as foreign, and the communication of this information to phagocytes, such as PMN leukocytes, in a manner that results in phagocytosis and destruction of the microbe.

Personnel: 1 GS-7 (9 months)
1 SP4 (6 months)

Funding: FY 79

Consumable Supplies \$1,465.00

PROGRESS

This approach has been highly successful with respect to realizing the protocol's objectives and is under continued investigation.

Status: Ongoing.

C-5-79 (Continued)

Allen, R.C. and Strong, G.F. The role of O_2 in phagocytosis and microbicidal action of polymorphonuclear leukocytes: an approach employing chemiluminescence. Presented at the 7th annual meeting of the American Society of Photobiology, 24-28 June 1979, Monterrey, Calif.

Allen, R.C.: Chemiluminescence: an approach to the study of the humoral-phagocyte axis in the host defense against infection. In "Liquid Scintillation Counting: Recent Applications and Developments" Vol. II (Peng, C.G., Horrocks D.L. and Alpen, E.L eds.), in press, Academic Press, New York.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Measurement of Cyclic Nucleotide Levels in Purified Populations of Lymphocytes Incubated with Mitogens.

WORK UNIT NO.: C-8-79

PRINCIPAL INVESTIGATOR: David G. Burleson, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS: John H. Sinegal, SSG

OBJECTIVES

To purify guinea pig lymphocytes on density gradients into functional subpopulations and measure intracellular levels of cyclic AMP and cyclic GMP after incubation of the purified cells with the mitogens for T and B cells.

TECHNICAL APPROACH

Lymphocytes are prepared from the spleen and lymph nodes of normal Harley guinea pigs. The lymphocytes are centrifuged in density gradients of colloidal silica coated with PVP (percoll) or subjected to centrifugal elutriation (Beckman JE-6 centrifuge rotor). Various fractions of the cell preparation are tested for their sensitivity to four mitogens; Phytohemagglutinin, Concanavalin A, lipopolysaccharide and pokeweed mitogen. Sensitivity to mitogen stimulation is measured by the amount of ^3H thymidine taken up by the cells during a 20 hour pulse started after 50 hours of culture and by the measurement of levels of cyclic AMP and cyclic GMP at 0-24 hours of culture. Cyclic nucleotide levels will be correlated with the amount of ^3H thymidine uptake measured in each fraction of cells.

Personnel: 1 SSG (4 months)

Funding: FY 79

Consumable Supplies \$3,075.70

PROGRESS

This is a new study. The cell culture system has been tested using the four mitogens. Optimum conditions for stimulation such as media, cell density, and pulse times have been established.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Studies on the Opsonization and Phagocytosis of Invasive and Noninvasive Shigella Species by Polymorphonuclear Leukocytes (PMNL).

WORK UNIT NO.: C-26-79

PRINCIPAL INVESTIGATOR: Gary S. Madonna, M.S., 1LT, MSC

ASSOCIATE INVESTIGATORS: Robert C. Allen, M.D., Ph.D., CPT, MC;
Michael M. Lieberman, Ph.D., CPT, MSC;
Dennis L. Stevens, M.D., Ph.D., LTC, MC

OBJECTIVES

To investigate the role of specific (postimmunization) sera in effecting opsonization and microbicidal action of PMNL against various invasive and noninvasive strains of Shigella sonnei and Shigella flexneri. The opsonic role of complement alone (alternative pathway) and in the presence of immune sera (classical pathway) will also be investigated.

TECHNICAL APPROACH

The invasive bacterial pathogens Shigella sonnei phase I and Shigella flexneri 2a "T" and their avirulent mutants S. sonnei phase II and S. flexneri 2a "O", respectively, are assessed for virulence using the Sereny test for keratoconjunctivitis in the guinea pig eye. Shigella antiserum is obtained from immunized rabbits and absorbed with various organisms to produce the desired specific antiserum. Immune serum is separated on a Sepharose 6B packed column after $(\text{NH}_4)_2\text{SO}_4$ precipitation or CM Affi-gel-blue (BioRad) treatment. Measurement of chemiluminescence (CL) is performed using a Beckman LS-150 scintillation counter.

Personnel: None

Funding: FY 79

Consumable Supplies \$254.00

PROGRESS

Using the phenomenon of CL, it was determined that specific antibody to S. sonnei phase I and complement are necessary for the opsonization

C-26-79 (Continued)

and phagocytosis of S. sonnei phase I by human PMNL. Removal of phase I antibodies by absorption or deletion of complement abolishes CL activity. Hence, it appears that phagocytosis of virulent S. sonnei by PMNL results after the organism has been labeled and identified by specific antibody with amplification of this recognition by the classical pathway of complement activation. However, recognition of phase II avirulent S. sonnei by PMNL does not require specific antibody. Complement alone provides recognition of phase II S. sonnei such that PMNL phagocytize these organisms resulting in CL. Increasing the concentration of complement simultaneously increases the CL response.

Preliminary CL results have shown the correlation of immune IgM and IgG fractions with CL. Additionally, we have shown that both IgM and IgG are effective in the CL responses in the presence of complement while only IgG is capable of this in the absence of complement.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Prostaglandin Synthesis Inhibitors on in vitro Suppressor Cell Activity in Lymphocytes from Patients with Common Variable Agammaglobulinemia.

WORK UNIT NO.: C-38-79

PRINCIPAL INVESTIGATORS: David G. Burleson, Ph.D., CPT, MSC; Michel N. Laham, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: John H. Sinegal, SSG

OBJECTIVES

To test the in vitro activity of prostaglandin synthesis inhibitors, such as indomethacin, on T-cell suppressor activity found in lymphocytes from patients with common variable agammaglobulinemia. The reversal of the suppressing activity on immunoglobulin cells by such inhibitors may indicate candidates for an effective therapeutic drug for this immunodeficiency.

TECHNICAL APPROACH

Lymphocytes from patients with common variable agammaglobulinemia will be cultured with normal cells to determine if there is a decrease in pokeweed mitogen induced immunoglobulin synthesis in normal cells. Immunoglobulins will be measured by radioimmunoassay and/or immunoglobulin secreting cells by plaque assay. Ig synthesis and Ig secreting cells will be measured and compared to controls.

Personnel: None

Funding:

PROGRESS

This is a new project, and it is too early to report any meaningful results.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Simultaneous Determination of Instantaneous Aortic Flow, High Fidelity Intracardiac Pressures, Intracardiac Phonocardiography, Echocardiographic Dimensions, and Derived Indices in Man.

WORK UNIT NO.: C-28-73

PRINCIPAL INVESTIGATOR: Joseph P. Murgo, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: John Paul Giolma, Ph.D., CPT, MSC; John Logsdon, M.D., MAJ, MC; Richard Davis, M.D., Ph.D., LTC, MC; George M. McGranahan, Jr., M.D., COL, MC

OBJECTIVES

1. To develop new techniques in cardiac catheterization, especially in the area of multi-solid state sensor catheters including high fidelity pressure sensors and electromagnetic flow meters. To utilize high speed biplane angiography and external echocardiography in conjunction with such techniques.
2. To utilize these techniques to define sophisticated parameters of ventricular function in patients with various cardiac diseases.
3. To develop specialized computer-assisted analyses of the data derived from such studies.
4. To quantitate left ventricular hydraulic output power.
5. To measure aortic and pulmonary artery input impedance by Fourier analysis and to determine the effect of changing physiologic states upon the impedance.
6. Detailed description of multiple specific objectives are to be found in the original protocol.

TECHNICAL APPROACH

All adult patients for routine right and left heart catheterization are evaluated in the usual manner by a cardiac fellow prior to catheterization. This evaluation includes strip chart echocardiography to determine the patient's suitability for certain aspects of the protocol. During catheterization, special, custom-designed, right and left heart

C-28-73 (Continued)

catheters are introduced into the right and left heart such that simultaneous high fidelity pressures are measured from the pulmonary artery, right ventricle, right atrium, left ventricle, and aorta. In addition, electromagnetically derived aortic and pulmonary flow velocities are recorded from the same sites that high fidelity pulmonary artery and aortic pressures are obtained. Patients are studied during both rest, supine exercise, and depending upon the patient's disease during a variety of other stresses or pharmacologic interventions. Some patients also undergo simultaneous external echocardiography during catheterization. The study is terminated after bi-plane ventricular angiography and coronary arteriography if indicated.

Personnel: 1 CPT (11 months)
1 GS11 (12 months)
1 SP5 (12 months)

<u>Funding:</u>	FY 79	FY 78
Consumable Supplies	\$ 698.75	
MEDCASE	\$99,434.89	\$7,399.04

PROGRESS

Continued progress in the multiple subprojects of this protocol have been experienced during FY 1979. Several new studies were presented and others initiated. Four papers have been accepted pending revision and two book chapters published.

Status: Ongoing.

Murgo, J.P., Alter, B.R., Dorethy, J.D., McGranahan, G.M. The dynamics of left ventricular ejection in obstructive and non-obstructive hypertrophic cardiomyopathy. Journal of Clinical Investigations (pending revisions).

Murgo, J.P., Westerhof, N., Giolma, J.P., Altobelli, S.A. Aortic input impedance in normal man: relationship to pressure wave shapes. Circulation (pending revisions).

Murgo, J.P., Westerhof, N., Giolma, J.P., Altobelli, S.A. Input impedance during exercise in man. Circulation Research (pending revisions).

Murgo, J.P., Westerhof, N., Giolma, J.P., Altobelli, S.A. Manipulation of ascending aortic pressure and flow wave reflections with the Valsalva maneuver: relationship to input impedance. Submitted to Circulation.

C-28-73 (Continued)

Murgo, J.P. Flow dynamics in hypertrophic cardiomyopathy. In "Cardiomyopathies", University of Tokyo Press (in press).

Westerhof, N., Murgo, J.P., Giolma, J.P. Systemic input impedance - theory, experimental results, and human measurements. Chapter 14 in "Engineering Principles in Cardiovascular Research," Editor H.C. Hwang, University Park Press, 1978.

Alter, B.R., Treasure, R.L., Martin, H.A., Humphrey, S.H., Murgo, J.P., McGranahan, G.M. Echocardiographic detection of a subannular aortic aneurysm. American Heart Journal, Vol 96, 4:525-528, October 1978.

Giolma, J.P., Murgo, J.P. Pulmonary artery input impedance in normal man. Proceedings of 31st Annual Conference of Engineering in Medicine and Biology, 16:354, October 1978.

Murgo, J.P., Giolma, J.P., Westerhof, N. Manipulation of aortic pressure and flow wave reflections with the Valsalva maneuver. Circulation, Supp. II, 58:290, 1978. Presented to the 51st Scientific Sessions of the American Heart Association, Dallas, Texas.

Murgo, J.P., Dorethy, J.F., Alter, B.R., McGranahan, G.M. Aortic valve gradients in normal man during exercise and isoproterenol infusion - relationship to pulsatile flow. Circulation, Supp II, 58:106, 1978. Presented to the 51st Scientific Sessions of the American Heart Association, Dallas, Texas.

Uhl, G.S., Felter, H.G., Logsdon, J.R., Murgo, J.P., McGranahan, G.M. Ventricular volume dependent changes in electromechanical delay. Circulation, Supp II, 58:291, 1978. Presented to the Scientific Sessions of the American Heart Association, Dallas, Texas.

Murgo, J.P., Giolma, J.P., Alter, B.R., Westerhof, N. Ascending aorta pressure waveshape - relationship to aortic input impedance. Circulation, Supp II, 58:620, 1978. Presented to the 51st Scientific Sessions of the American Heart Association, Dallas, Texas.

Bowers, R.E., Murgo, J.P., Felter, H.G., McGranahan, G.M. Exercise induced changes in splitting of the second heart sound in normal man. Circulation, Supp II, 58:285, 1978. Presented to the 51st Scientific Sessions of the American Heart Association, Dallas, Texas.

Murgo, J.P. Chairman session on Clinical Research - Laennec Society, 51st Scientific Sessions of the American Heart Association, Dallas, Texas, November 1978.

Murgo, J.P. Panel member, 28th Annual Sessions of the American College of Cardiology. Physiologic basis of heart sounds and murmurs. Miami, Florida, March 1979.

C-28-73 (Continued)

Murgo, J.P. Visiting consultant, Presbyterian Hospital and University of Texas Health Science Center, Dallas, Texas, April 1979.

- a. Hemodynamic profile of the cardiomyopathies.
- b. Hemodynamics of pericardial tamponade.

Murgo, J.P. Research seminar series, University of Texas Health Science Center at San Antonio, Injection dynamics in obstructive and nonobstructive hypertrophic cardiomyopathy, June 1979.

Murgo, J.P. Grand Rounds, University of Texas Health Science Center at San Antonio. Hemodynamic profile of the cardiomyopathies, September 1979.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Outpatient Algorithm Validation - A Pilot Study.

WORK UNIT NO.: C-9-75

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if clinical outpatient algorithms originally used to treat civilian outpatient populations can be validated and improved in a military outpatient environment - a Phase I Study.

TECHNICAL APPROACH

Patients treated and evaluated by algorithm-directed AMOSISTS and ready to leave the clinic are randomized to either re-evaluation by a staff physician or to go home on the recommended therapy. Those seen by the staff physician are evaluated without knowledge of the results of their AMOSIST evaluation. Outcome follow-up of both groups takes place at a central point after their index visit. Computer analysis of the collected data allows outcome comparisons of patients treated by AMOSISTS with those treated by physicians, an analysis of the usefulness of laboratory evaluations, and redesign of the algorithms used by the AMOSISTS.

Personnel: None.

Funding: None.

PROGRESS

To date a new URI algorithm has been developed, tested, and is being currently used. Likewise, algorithms for headache, back pain, and extremity trauma have been shown to be safe and effective in the hands of BAMC AMOSISTS. Algorithms currently under study include those for nausea/vomiting/diarrhea, female dysuria/vaginal discharge, and ankle trauma.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Measurement of Transepidermal Water Loss in Anhidrotic Ectodermal Dysplasia and Erythroderma.

WORK UNIT NO.: C-29-75

PRINCIPAL INVESTIGATOR: Robert L. Rietschel, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Richard L. DeVillez, M.D., LTC, USAR

OBJECTIVES

1. To measure total body evaporative water loss in skin conditions of excessive and insufficient transepidermal water loss and compare these values with measurements of water loss from small areas of skin.
2. To study the effect of various topical compounds in common dermatologic use on transepidermal water loss in individuals with excess or insufficient water loss.

TECHNICAL APPROACH

A stream of dry nitrogen gas is blown across the skin surface and then into an electrolytic moisture analyzer. The amount of moisture present is detected and expressed in $\text{mg}/\text{cm}^2/\text{hr}$.

Personnel: None.

Funding: FY 79

Rental \$27.00

PROGRESS

The dynamics of heat loss by two patients with classic anhidrotic ectodermal dysplasia were studied. Both were active in high school athletics and avoided heat injuries by various forms of behavior modification.

C-29-75 (Continued)

Elevated core and skin temperature measurements were found at rest in comfortable environments. In a warm environment 35-45% of the heat generated was lost by radiation, 44-52% by conduction and convection, and only 4-6% by evaporation. Heat loss in control subjects was 9% by radiation, 17% by conduction/convection, and 67% by evaporation. The dry routes of heat dissipation used by the anhidrotic patients were inadequate to prevent a rise in core temperature.

Status: Ongoing.

Rietschel, R.L. A method to evaluate skin moisturizers in vivo. Submitted to Journal of the Society of Cosmetic Chemists.

Rietschel, R.L. Skin moisturization without occlusion. Submitted to Cutis.

Rietschel, R.L. A method to evaluate skin moisturizers in vivo. Presented to the Society of Cosmetic Chemists, 3 May 1979, Dallas, Texas.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Quantitative Studies of Phagocytosis - The Use of Acridine Orange (AO) as an Indicator of Phagocytic Ingestion and Bactericidal Effects.

WORK UNIT NO.: C-9-76

PRINCIPAL INVESTIGATOR: Dennis L. Stevens, M.D., Ph.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the phagocytosis of polymorphonuclear leukocytes of acridine orange stained bacteria, and to develop a simple, reliable assay of this process which will be amenable to clinical laboratory utilization.

TECHNICAL APPROACH

Acridine orange stained E. coli were fed to human granulocyte suspensions and the fluorescence spectra recorded at different incubation times. A new Aminco Bowman R136 photomultiplier tube was utilized.

Personnel: None

Funding: None

PROGRESS

As indicated in the annual report of FY 78, acridine orange fluorescence of bacteria ingested by human PMNL is dependent upon a) the pH of the phagolysosome, b) the concentration of the dye within the phagolysosome, and c) incubation time.

C-9-76 (Continued)

Since acridine orange, like gentamicin, is a basic anion, it is concentrated within acidic phagolysosomes at a rate proportional to the (hydrogen ion) concentration difference between cytoplasmic and phagolysosome contents. The pH of the phagolysosome is dependent upon a) lactic acid accumulation, b) hydrogen pump (the inner layer of phagolysosome membrane is in fact derived from the outer aspect of the cell cytoplasmic membrane), and c) other hydrogen ion yielding reactions related to granulocytic-phagolysosome metabolism.

Thus, the change in visible fluorescence of ingested bacteria from green to orange cannot be construed as a loss of viability of the organism. Nevertheless, measurement of qualitative shifts in fluorescence (green to red) may well be a useful indicator of phagocytosis induced intracellular granulocytic microbicidal activity.

Since the above report, no work has been done on this study, and, therefore, it is terminated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Demonstration of a Testosterone Binding Protein in Semen.

WORK UNIT NO.: C-23-76

PRINCIPAL INVESTIGATOR: Albert Thomason, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To demonstrate a testosterone binding protein in semen.

TECHNICAL APPROACH

Attempts are being made to demonstrate a specific binding protein by using polyacrylamide gel electrophoresis and radioactive testosterone. Two approaches have been used so far: 1) To add the radioactive testosterone to the semen before the electrophoresis and then to count consecutive sections of the gel to see if any of the sections contained high counts; and 2) To place the testosterone directly into the gel and subsequent to the electrophoresis to section the gel into consecutive equal segments.

Personnel: None.

Funding: None.

PROGRESS

To date no testosterone binding protein has been isolated. In the coming year an effort will be made to use C¹⁴ labeled testosterone instead of T₃ labeled testosterone.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Hemodynamic Effects of Angiographic Contrast Material with Dynamic and Static Exercise.

WORK UNIT NO.: C-3-77

PRINCIPAL INVESTIGATOR: Joseph P. Murgu, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the usefulness of postangiographic hemodynamic data in assessing left ventricular function by comparison with the effects of standard forms of left ventricular stress in the cardiac catheterization laboratory.

TECHNICAL APPROACH

Following left ventriculography performed at the time of cardiac catheterization, serial measurement of the following parameters was made: pulmonary capillary wedge, pulmonary arterial, right ventricular, right atrial, left ventricular, and aortic pressures; serial thermal dilution cardiac outputs; pulmonary artery and aortic flow velocity signals. These parameters were then compared to those obtained in the resting and steady exercise states. In order to carry out the project, a special high fidelity left ventricular injection catheter has been designed.

Personnel: None.

Funding: None

PROGRESS

Some problems are still being encountered with the performance of the special high fidelity injection catheter.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Mechanism of the Modulation of Lymphocyte Functions by Complement.

WORK UNIT NO.: C-6-77

PRINCIPAL INVESTIGATOR: Michel N. Laham, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: David G. Burleson, Ph.D., CPT, MSC; Gwen L. Wright, SP5

OBJECTIVES

To determine the mechanism of the modulation of lymphocyte proliferative responses by the early complement components, especially C₂.

TECHNICAL APPROACH

Human peripheral blood lymphocytes are cultured in complement-free medium, stimulated with various mitogens and antigens in microtiter plates, and their uptake of tritiated thymidine is measured after 3-5 days of culture. The effect of complement in that system is determined by preincubating the cells with individual purified human complement components (Cordis Lab.) prior to culture.

Personnel: 1 SFC (6 months)
1 SP5 (6 months)

<u>Funding:</u>	FY 79	FY 78
Consumable Supplies	\$187.35	\$1,257.30

PROGRESS

Many of the original objectives of our project have been reached. We now know that in doses up to 1,000 e.m. per lymphocyte, the early complement components (C₁, C₄ and C₂ together) enhance the cells responses to mitogens and antigens. Higher doses of complement progressively inhibit lymphocyte responses to mitogens but continue to enhance their

C-6-77 (Continued)

stimulation with antigen. These effects are removed by prior heat inactivation of the complement. They persist when the cells are preincubated with C_{142} for 1 hour, then washed prior to addition of mitogen. Fluid-phase C_1 is required, suggesting the modulatory effect of C_{142} is mediated by a product of the fluid-phase of cleavage of C_2 . Finally, the effect correlates best with the amount of C_2 added to the cell cultures, once a minimum amount of C_1 and C_4 (250 e.m.) is present.

Since this project was initiated, C_2 deficiency has been found by others to be associated with HLA A_{10} , B_{18} and LD_{7a} . This suggests that the gene controlling the synthesis of C_2 is closely linked to the major histocompatibility complex (MHC). Patients with C_2 deficiency have also been found to have an increased incidence of autoimmune disease, especially lupus. This implies that C_2 itself may be involved in the afferent phase of the immune response, i.e. in immune recognition and self-tolerance. Our findings anticipated these developments in the literature.

From this point on, we will attempt to define the effect of C_2 , in both its native and active forms, on mixed lymphocyte reactions. We will endeavor to determine the exact site of action of C_2 and whether it can be detected on the cell surface by direct and indirect immunofluorescence. We will attempt to uncover its precise mechanism of action by blocking translation and protein synthesis, respectively, and observing the effect of such maneuvers on lymphocyte modulation by C_2 . Finally, since C_2 may well exert its effect primarily via suppressor T cells, we will use the methods outlined in project C-38-79 to detect the activity of such cells in our system. We will also look directly at the effect of C_2 on PWM-induced immunoglobulin synthesis using these same methods.

Status: Ongoing.

Laham, M.N., Panush, R.S. and Caldwell, J.R. Modulation of lymphocyte proliferative responses to mitogens and antigens by complement components C_1 , C_4 and C_2 . Submitted to Journal of Clinical Investigation.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Prospective Study of the Usefulness of the Chest X-Ray in
Evaluating Patients with Acute Cough.

WORK UNIT NO.: C-19-77

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: N. Joe Thompson, M.D., LTC, MC

OBJECTIVES

To determine if the use of the chest x-ray is cost-effective in the evaluation of ambulatory patients presenting with an acute cough at BAMC; to determine the value of clinical signs and symptoms and the clinician's judgment in predicting the presence of infiltrate on the chest x-ray; and to compare cough patients evaluated with a chest x-ray with cough patients evaluated without a chest x-ray in terms of clinical outcome and the cost of care.

TECHNICAL APPROACH

The patients presenting to the BAMC ER/AMIC with complaints including acute coughs were selected for the study. Those selected received a standardized history and physical examination, and all received chest x-rays. Physicians seeing these patients were asked to request chest x-rays as they felt clinically indicated, but were randomly shown both x-rays they did and did not request. A four week outcome study was carried out on each patient following his discharge from the clinic. Computer analysis allows search for combinations of historical and physical findings at index visit which are predictive of x-rays which result in changes in the clinicians behavior.

Personnel: None.

Funding: None.

PROGRESS

The data collection phase of this project has been completed. The data are currently being analyzed. Preliminary inspection of the data reveals

C-19-77 (Continued)

that chest x-rays in this clinical situation are rarely a factor in changing physicians clinical plans. If this preliminary finding "holds up" it will result in a change in our utilization of chest x-rays in the emergency department.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of the Effectiveness of Oral Methoxsalen Followed by Longwave Ultraviolet Light (UVA 320-400 nm) in the Treatment of Psoriasis.

WORK UNIT NO.: C-23-77

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of 8-methoxypsoralen (methoxsalen) and longwave ultraviolet light (PUVA) in the treatment of psoriasis.

TECHNICAL APPROACH

Patients are given a prescribed dosage of 8-methoxypsoralen two hours prior to long-wave ultraviolet light exposure. The amount of light energy applied to the skin is gradually increased to obtain clinical clearing of the skin disease and to promote pigmentation (tanning) of the skin. The eyes are protected by special ultraviolet glasses that block out penetration of ultraviolet. The light dosage is carefully regulated to prevent a sunburn reaction of the skin. All patients receive initial laboratory screening studies and ophthalmologic evaluation and follow-up examinations at regular intervals.

Personnel: None.

Funding: None.

PROGRESS

Since our last progress report, 22 patients with psoriasis have entered into our PUVA study with generally good to excellent results. Acute side effects have been few and minor. One of our patients developed a basal cell carcinoma on the forehead, but none have developed squamous cell carcinoma (which is the biggest concern) or melanoma. New patients will continue to be entered into the study based on clinical condition and extent of disease as outlined in the protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Toxicity of Aminoglycosides to Kidney Tumor Cell Lines in Tissue Culture.

WORK UNIT NO.: C-26-77

PRINCIPAL INVESTIGATOR: James M. Boyd, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Deborah Hunter, SP5

OBJECTIVES

To establish various kidney tumor cell lines in vitro and to test the efficiency of kill of these tumor lines with various aminoglycosides.

TECHNICAL APPROACH

The tumor cell lines were obtained. All were malignant, and all were derived from the Syrian hamster. These have been characterized as to population doubling time, cloning efficiency, and saturation density.

Personnel: 1 SP5 (3 months)

Funding: None.

PROGRESS

This protocol was initiated in order to establish tissue culture capabilities in the Clinical Investigation Service. This has been accomplished, and therefore, this study is considered completed.

Status: Completed.

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Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Radiotherapy on Regional Lung Function in Patients with Bronchogenic Cancer.

WORK UNIT NO.: C-36-77

PRINCIPAL INVESTIGATOR: Peter S. Kennedy, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Stephen Sorgen, M.D., MAJ, MC; A. Baker, M.D., LTC, MC; Charles Brearley, M.D., MAJ, MC

OBJECTIVES

1. To evaluate regional lung function in patients with localized, unresectable bronchogenic cancer by means of radionuclide lung scans, plus selected pulmonary function tests.
2. To compare regional lung function in patients before and serially after therapeutic super voltage irradiation in an attempt to correlate changes in RLF with response to treatment, respiratory symptoms, local disease control, and survival.

TECHNICAL APPROACH

Patients with unresectable bronchogenic cancer who are candidates for primary treatment by cobalt irradiation undergo Xenon-Technesium Ventilation-Perfusion lung scans and selected pulmonary function tests. These studies along with clinical evaluation and standard P.A. chest x-ray will be repeated serially. Changes in the results of these tests will be correlated with tumor response and recurrence patterns.

Personnel: None

Funding: None

PROGRESS

Dr. Kennedy and Dr. Sorgen, the two physicians involved in this project, are no longer at BAMC, and there is no interest from other physicians. Therefore, the project is terminated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Algorithm Directed Troop Medical Care (ADTMC) Project.

WORK UNIT NO.: C-46-77

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: 1st Cavalry Division Surgeon and Staff, Fort Hood, TX; Staffs of Troop Medical Clinics 5, 7, and 8, Fort Hood, TX

OBJECTIVES

To take existing algorithm directed triage and health care delivery systems, adapt them to a combat arms troop environment, and test the hypothesis that medical treatment/return to duty of soldiers who need to be seen at military sick call can be expedited with no decrease in the quality of medical care provided.

TECHNICAL APPROACH

This project introduced an algorithm-directed care system into the care of active duty military personnel and was to be studied by comparison at each phase of the implementation of the test unit with a control unit receiving medical care in a standard format.

Personnel: None.

Funding: None.

PROGRESS

At best, progress in this area is slow moving. We have demonstrated the efficacy and safety of algorithm-directed troop triage to be carried out by the most junior 91-B medics in the Army Medical Department. We are in the process of trying to see whether or not such care can be administratively implemented in field settings at Fort Sill and Fort Hood.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Tetracycline-induced Ultraviolet Fluorescence of Pathologic
Pulmonary Tissues as Viewed Through the Fiberoptic Bronchoscope.

WORK UNIT NO.: C-1-78

PRINCIPAL INVESTIGATOR: Robert B. Blumer, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To establish whether in vivo tetracycline labeling can be used to aid the endoscopist in locating pathologic pulmonary tissues when viewed through a fiberoptic bronchoscope incorporating an ultraviolet light source.

TECHNICAL APPROACH

Patients undergoing bronchoscopy for diagnostic purposes will be given tetracycline for four days prior to bronchoscopy. Tetracycline will be discontinued for at least 24 hours prior to the procedure. Examination will be carried out at bronchoscopy, first using incandescent light source, and if no abnormalities are noted, an ultraviolet light source will be inserted and re-examination performed. Any areas which fluoresce under ultraviolet light will be biopsied, and records will be kept to determine the diagnostic value of the procedure.

Personnel: None.

Funding: None.

PROGRESS

The ultraviolet light source has been ordered. The project awaits receipt of this before selecting patients and proceeding with the study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Sodium Nitroprusside Infusion on Hemoglobin Oxygen Carrying Patterns in Man.

WORK UNIT NO.: C-5-78

PRINCIPAL INVESTIGATOR: Stephen H. Humphrey, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the effect of sodium nitroprusside infusion on the ability of hemoglobin to carry oxygen.

TECHNICAL APPROACH

The effect of intravenous sodium nitroprusside (SNP) was studied in three patients who required prolonged infusions of SNP. Hemoglobin (H) and methemoglobin (M) concentrations were measured spectrophotometrically, and the O₂ content (C) of fully oxygenated blood was measured using the Van Slyke apparatus before and during SNP infusion. HOC was calculated by subtracting dissolved O₂ from C, then dividing by H.

Personnel: None.

Funding: None.

PROGRESS

Changes in HOC appeared inversely related to the rate of SNP infusion. Maximum decreases ranged from 0.13 to 0.32 cc O₂/gm H (8.5-23%). Concentrations of M did not change. SNP has the potential to reduce HOC, an effect not explained by M formation. This may result in a decrease in O₂ which can be transported to tissues and should be considered in critically ill patients.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Minoxidil as an Anti-Hypertensive in Patients Refractory to Available Medications.

WORK UNIT NO.: C-6-78

PRINCIPAL INVESTIGATOR: Paraic Mulgrew, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if minoxidil is an effective alternative treatment for patients whose blood pressure is refractory to available drugs or who have experienced unacceptable side effects from them and whose situation is life-threatening.
2. To document clinical experience with this drug.

TECHNICAL APPROACH

Minoxidil will be administered as recommended by the drug company protocol.

Personnel: None.

Funding: None.

PROGRESS

The one patient entered on the study was transferred to Wilford Hall USAF Hospital for renal transplantation. Up until that time Minoxidil was effective in controlling blood pressure in this patient as determined by daily cuff measurements. Side effects of hirsutism were experienced by patient. The patient died following transplantation from gram negative sepsis - unrelated to medication in question.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Serum ACTH Levels in Lung Cancer Patients.

WORK UNIT NO.: C-10-78

PRINCIPAL INVESTIGATOR Merrill S. Kies, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Sherwyn L. Schwartz, M.D.

OBJECTIVES

1. To determine if serum ACTH levels are abnormally elevated in lung cancer patients.
2. To determine if elevated serum ACTH levels correlate with disease recurrence in lung cancer patients who have undergone attempted curative surgical resection.
3. To determine if serum ACTH levels correspond to clinical disease activity in patients with oat cell carcinoma treated medically.

TECHNICAL APPROACH

ACTH levels in two groups of lung cancer patients and controls will be studied. Group A will consist of 20 consenting patients with histologically proven oat cell carcinoma of the lung. Group B will be composed of 20 patients considered for definitive surgical treatment of suspected or proven primary non-oat cell lung cancer. If no malignancy is found at surgery, the patient will enter the control group. Group C will be composed of patients undergoing exploratory thoracotomy for suspected lung cancer who at surgery are not found to have lung cancer.

Pretreatment ACTH levels will be obtained on all patients. In Group A patients, a second assay will be obtained if the patient achieves a complete remission of all clinical evidence of disease. Serial ACTH levels will thereafter be obtained every 2 months until relapse occurs. Group B patients will have ACTH levels performed at 4 weeks postoperatively and, again if clinical relapse occurs.

Personnel: None.

Funding: None.

C-10-78 (Continued)

PROGRESS

Serum samples before and after induction treatments have now been collected on approximately 35 lung cancer patients of various histologies. These samples have been forwarded to Dr. Jack Allen of the University of Illinois, Neuroendocrine Section, Peoria, Illinois. At this time, ACTH assays are being performed. Dr. Allen has indicated that he would be very interested in performing other hormonal assays on the samples, probably including calcitonin, substance S, prolactin and perhaps, polyamine levels.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Bacterial Antibiotic Resistance Mediated by Plasmids - Demonstration and Characterization of Plasmids as Epidemiologic Markers.

WORK UNIT NO.: C-13-78

PRINCIPAL INVESTIGATOR: Francis O'Donnell, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Dennis L. Stevens, M.D., LTC, MC

OBJECTIVES

To document the role of plasmids in mediating antibiotic resistance in clinical isolates of Klebsiella pneumoniae and other gram negative bacteria, and to characterize the plasmids in terms of molecular weight using agarose gel electrophoresis, with a view to using such information in the epidemiologic study of serious nosocomial infections caused by antibiotic resistant bacteria.

TECHNICAL APPROACH

1. Verification of antibiotic resistance patterns of Klebsiella pneumoniae isolates.
2. Attempt to "cure" Klebsiella isolates of the plasmids thought to mediate antibiotic resistance.
3. Attempt to transfer the plasmids via bacterial conjugation with recipient bacteria.

Personnel: None.

Funding: None.

PROGRESS

Antibiotic resistance patterns of Klebsiella pneumoniae isolates have been verified. "Curing" was attempted via incubation at 44°C. Replica plating technique was used to detect bacteria which had lost their

C-13-78 (Completed)

resistance to antibiotics. No curing was demonstrated. Use of other curing techniques was not begun based upon a decision to move on to method "3". A strain of E. coli (C600) was obtained from Dr. Moody, University of Texas Health Science Center at San Antonio. This strain proved to be well suited as a recipient of plasmids transferred by conjugation.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Amantadine in the Prophylaxis of Influenza A/USSR/77

WORK UNIT NO.: C-14-78

PRINCIPAL INVESTIGATOR: David W. Potts, M.D., MAJ, USAF MC

ASSOCIATE INVESTIGATORS: Dennis L. Stevens, M.D., LTC, MC; Theodore R. McNitt, M.D., LTC, MC

OBJECTIVES

To document the clinical and epidemiologic characteristics of influenza A/USSR/77 infection in a young adult population and evaluate the effect of amantadine on the incidence, duration and clinical manifestations of influenza infection, and on the subclinical infection rate.

TECHNICAL APPROACH

A group of young adult soldiers (age 18-24 years) living in two separate dormitories/barracks were randomly divided into two groups, one of which received amantadine, 100 mg BID for three weeks, following initial occurrence of influenza-like illness in association with A/USSR/77 virus isolations. A second group of equal size was given a placebo BID for three weeks.

In order to document the possible presence of A/Texas/- or A/Victoria-like viruses, as well as A/USSR/77 viruses, nose and throat cultures were taken from all subjects.

A 10 ml blood sample was taken at the start of the study from all participants, and a post-epidemic serum was collected 2-3 weeks after the epidemic ended. Serologic testing documented which strains of virus infected the subjects and what the clinical and subclinical infection rate was in treated and untreated individuals.

Personnel: None.

Funding: None.

C-14-78 (Continued)

PROGRESS

The study established the safety of amantadine; difficulty concentrating and insomnia were the only side effects observed significantly more often among recipients of amantadine. The small number of participants in the study and the low overall incidence of infection with influenza virus precluded a definitive conclusion that amantadine was effective in reducing the incidence and severity of disease in those infected with influenza A/USSR/77.

Status: Ongoing.

Potts, D.W.; Kantro, R.J.; McNitt, T.R.; and Jocz, R.J. Influenza 1978. Southern Medical Journal 72,2:139-140, February 1979.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Etiology of Postpericardiotomy Syndrome.

WORK UNIT NO.: C-17-78

PRINCIPAL INVESTIGATOR: Dennis L. Stevens, M.D.LTC, MAJ, MC

ASSOCIATE INVESTIGATORS: Larry D. Hudson, M.D., CPT, MC; Richard C. Traugott, M.D., LTC, MC

OBJECTIVES

To determine the etiology of postpericardiotomy syndrome.

TECHNICAL APPROACH

Serum specimens were obtained from 78 patients admitted to the thoracic surgery service for coronary artery surgery or valve replacement. Pre-surgical as well as discharge serum specimens were obtained on all patients. Fifteen patients developed postoperative symptoms and signs suggestive of postpericardiotomy syndrome defined in the protocol. Additional serum specimens were obtained from these patients at a time when they were symptomatic. Serum specimens were screened for antinuclear antibody using the FIAXTM fluorospectrophotometric assay. Cell specimens were negative for ANA. Next, thin sections from operative specimens (myocardium and pericardium) were prepared, incubated with each of the serum specimens and then washed and stained with anti-human IgG or IgM. Fluorescence patterns were studied using the Zeiss Epi-transmitted Fluorescence Microscope.

Personnel: None.

Funding: None.

PROGRESS

In addition to the negative ANA reactions on all serum specimens, a total of 20 patient sera were evaluated for anti-pericardial or anti-myocardial antibody. On all of these patient's sera the background

C-17-78 (Continued)

fluorescence was strong regardless of their clinical course. Technically, it became obvious that frozen tissue was unacceptable as a substrate for the fluorescence demonstration of antibody against said tissue. In short, the tissue itself was fluorescent when exposed to UV light. Further studies should be directed at using fresh rabbit or rat myocardial or pericardial tissue as a substrate in order to reduce the "nonspecific artifact" induced by freezing human cardiac tissue.

This investigation has neither proven nor disproven the hypothesis that the post-pericardiotomy syndrome is due to the development of anti-myocardial or anti-pericardial antibody.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Controlled Study of the Effects of High Dose Corticosteroids Versus Medium Dose Corticosteroids in the Management of Acute Asthma.

WORK UNIT NO.: C-19-78

PRINCIPAL INVESTIGATOR: Glenn L. Bugay, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Roy S. Adaniya, M.D., MAJ, MC; Susan Marshall, M.D.

OBJECTIVES

1. To compare the efficacy of high dose corticosteroids (loading dose of 1 gm. of methylprednisolone followed by 500 mg. I.V. q6h) versus medium dose corticosteroids (loading dose of 60 mg. of methylprednisolone followed by 20 mg. I.V. q6h) on acute asthmatic attacks. Objective parameters to be compared include changes in PFT's and ABG's.
2. To compare complications of high dose corticosteroids versus medium dose corticosteroids.

TECHNICAL APPROACH

The study group will consist of adult patients with asthma whose symptoms remain unchanged while on therapeutic dose of methyl xanthines and sympathomimetics. The dosage of corticosteroids will be double blinded by the pharmacy service - 10 patients receiving medium dose, as defined in the objectives, and 10 patients receiving high dose.

Personnel: None.

Funding: None.

PROGRESS

The study was terminated due to insufficient number of evaluable patients.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Aspirin Administration on Mortality in Infected Rats.

WORK UNIT NO.: C-20-78

PRINCIPAL INVESTIGATOR: David W. Potts, M.D., MAJ, USAF MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Dennis L. Stevens, M.D., LTC, MC; Michael M. Lieberman, Ph.D., CPT, MSC; Bryon Wilson, D.V.M., MAJ, VC

OBJECTIVES

To study the effects of aspirin administration on an infected mammalian model.

TECHNICAL APPROACH

Twenty-two matched 200 to 250 gm white rats were studied. The rats were divided into four groups. Group 1 (six rats) received a single subcutaneous injection of 0.5 cc of tryptic soy broth (TSB) with 4×10^8 Pseudomonas aeruginosa per cc followed by injections of 0.3 cc of normal saline with 100 mg/cc sodium salicylate every six hours. Group 2 (six rats) were injected with an identical dose of Pseudomonas and 0.3 cc of normal saline without salicylates. Group 3 (five rats) received TSB and sodium salicylate, and group 4 (five rats) received TSB and normal saline.

Personnel: None.

Funding:

	FY 78	FY 79
Consumable Supplies	\$513.30	\$1,058.00

PROGRESS

The rats in both Groups 1 and 2 developed a temperature of 40°C at six hours. However, the rats in Group 1 became euthermic by 18 hours while those in Group 2 remained febrile over 40°C throughout the 48 hours of observation. All rats in Groups 3 and 4 remained euthermic.

C-20-78 (Continued)

All rats in Group 1 died within 48 hours. Five of the six rats in Group 2 survived. All of the rats in Groups 3 and 4 survived. In this model, fever is beneficial to the host's survival.

Status: Completed.

Potts, D.W., McNitt, T.R., and Stevens, D.L. Therapeutic Effect of Fever on Infected Rats. Abstract submitted for consideration for presentation at the American Society of Microbiology meeting, October 1979.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Benzoyl Peroxide in the Treatment of Superficial Mycoses.

WORK UNIT NO.: C-24-78

PRINCIPAL INVESTIGATOR: John J. Lucas, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Robert L. Rietschel, M.D., MAJ, MC; Charles
W. Lewis, M.D., COL, MC

OBJECTIVES

To evaluate the efficacy of benzoyl peroxide in a double blind study comparing the active agent against its vehicle in the treatment of various superficial fungal infections. These will include tinea versicolor, tinea corporis, tinea pedis, tinea cruris, and tinea unguinum.

TECHNICAL APPROACH

A double blind compared study for the efficacy of benzoyl peroxide in the treatment of the above fungal infections will be carried out. A commercial benzoyl peroxide will be paired against its vehicle. Patients will be cultured for fungi before and during the study.

Personnel: None.

Funding: None.

PROGRESS

Even though an IND number was issued in May 1978, final approval is still pending.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Antibody Response to Pneumococcal Vaccine in Adult Patients
with Malignant Disease.

WORK UNIT NO.: C-26-78

PRINCIPAL INVESTIGATOR: Richard A. Shildt, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: James Boyd, M.D., MAJ, MC; Ronald Rubin, M.D.,
MAJ, MC; J. Dean McCracken, M.D., LTC, MC

OBJECTIVES

1. To compare antibody responses in a population of oncology patients immunized with pneumococcal vaccine with that of normal controls.
2. To further clarify the optimum time to immunize patients receiving cytotoxic agents.
3. To obtain baseline data regarding efficacy of pneumococcal vaccine in selected patient populations.

TECHNICAL APPROACH

One-hundred-forty patients have been vaccinated with Pneumovax and antibody titers determined.

Personnel: None.

Funding: None.

PROGRESS

The results are being analyzed.

Status: Ongoing.

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BROOKE ARMY MEDICAL CENTER FORT SAM HOUSTON TEX
ANNUAL RESEARCH PROGRESS REPORT, FISCAL YEAR 1979, (U)
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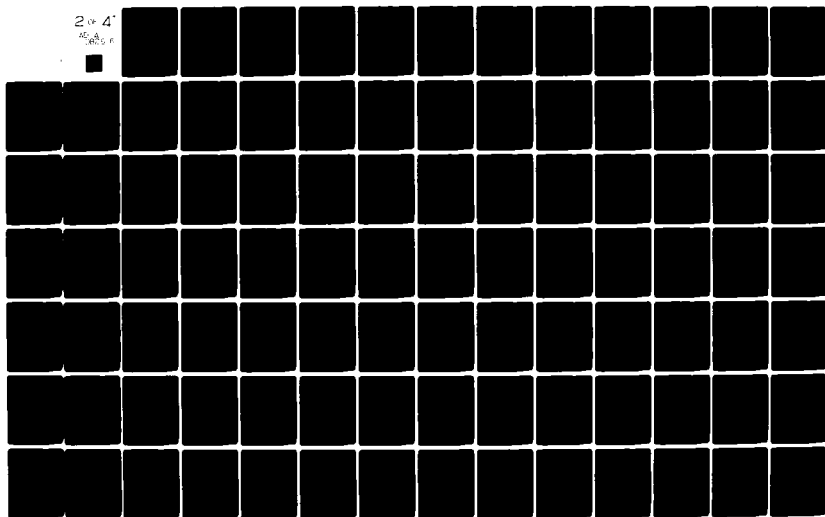
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AD-A082 516



DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Noninvasive Radioisotope Measurement of Esophageal Acid Clearance.

WORK UNIT NO.: C-2-79

PRINCIPAL INVESTIGATOR: N. Joe Thompson, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if abnormalities of esophageal acid clearance can be correlated with clinical symptoms of peptic esophagitis.

TECHNICAL APPROACH

The study will include two groups of individuals who will be defined as "normal" and "abnormal". The "normal" group will be free of heartburn and symptoms of gastroesophageal reflux by history. The "abnormal" group will have historical evidence of gastroesophageal reflux. Each individual in the "normal" group will have a radioisotopic esophageal clearance test (RECT). Those in the "abnormal" group will undergo the standard acid reflux test (SART), measurement of lower esophageal sphincter (LES) pressure, esophageal motility (EM), and other diagnostic tests as part of their routine clinical care.

Personnel: None

Funding: None.

PROGRESS

This project was not pursued because of other duty commitments.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Growth of Human Tumor Cell Colonies in Soft Agar.

WORK UNIT NO.: C-6-79

PRINCIPAL INVESTIGATOR: James. F. Boyd, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To establish a tissue culture lab for the growth of human stem cells in soft agar culture. Growth patterns and growth requirements will be observed.

TECHNICAL APPROACH

Samples of malignant tissue are obtained directly from patients, dispersed in a single cell suspension, and plated in a 0.3% agar overlayer with a 0.5% agar feeder underlayer. The percentage of stem cells per 5×10^5 cells is determined by the number of colonies which grow per 5×10^5 cells plated.

Personnel: 1 SP5 (6 months)

Funding: FY 79

Consumable Supplies \$800.00

PROGRESS

Growth of ovarian and melanoma colonies in vitro has been successful. These samples have been obtained from malignant effusions. The major problem has been in obtaining single cell suspension in spite of heparinization of the samples. This may be due to the use of Hank's balanced salt solution containing calcium and magnesium.

Status: Transferred to Eisenhower Army Medical Center.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Systemic Gonococcal Infections

WORK UNIT NO.: C-7-79

PRINCIPAL INVESTIGATOR: David W. Potts, M.D., MAJ, USAF MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., LTC, MC; Dennis L. Stevens, M.D., LTC, MC; Michael M. Lieberman, Ph.D., CPT, MSC

OBJECTIVES

To answer the questions: (a) Will standard blood culture media support the rapid growth of small numbers of Neisseria gonorrhoeae; will the addition of Isovitalex increase the sensitivity or rapidity of isolation of Neisseria gonorrhoeae from blood culture media? (b) Are current strains of Neisseria gonorrhoeae sensitive to semi-synthetic penicillins?

TECHNICAL APPROACH

Fifteen strains of Neisseria gonorrhoeae were used. Ten strains were local clinical isolates. Three of these were from patients with disseminated disease including BB, one from a cervical culture and six from urethral cultures. Various media were tested for their ability to support the growth of Neisseria gonorrhoeae. The organism was routinely sub-cultured from EVAC-TSB.

Personnel: None.

Funding: FY 79

Consumable Supplies \$1,058.00

PROGRESS

In six strains of Neisseria gonorrhoeae tested, IsoVitalex did not change the rate or frequency of recovery in any media. Only one of the eight strains of Neisseria gonorrhoeae tested could be recovered from anaerobic thiol and then only from the bottle with the highest (10^5 CFU) inoculum. The IsoVitalex and thiol limbs were no longer used after six and eight strains were tested respectively.

C-7-79 (Continued)

With an inoculum of 10^5 CFU per bottle, organisms could be recovered from all ANM and E-VAC TSB cultures but from only 84% of Difco TSB. At 10^3 CFU per tube, 100% of strains were recoverable in E-VAC TSB but the number of strains recoverable in Difco TSB decreased to 46%, while the number recoverable in ANM decreased to 73%. At 10^2 CFU per tube, recovery was lower from all media but the biggest drop was with Difco TSB from which only 17% of strains were recoverable. At 72 hours, the percent recoverability improved in all media. However, at 10^3 CFU per tube, 31 and 13% of strains remained unrecoverable in Difco TSB and ANM media respectively. While at 10^2 CFU per tube, 42 and 33% were not recovered. Recovery of all strains from E-VAC TSB was possible even at 10^2 CFU per bottle. No further recovery occurred when cultures were incubated for seven days.

Different strains of Neisseria gonorrhoeae were recovered from ANM and Difco TSB. At 72 hours, only a single strain from a urethral discharge was not recoverable in either ANM or Difco at 10^2 CFU per tube. Type specific recovery rates could not be identified. Strains which had been isolated from patients with local disease were not recovered with a different frequency than those isolated from patients with disseminated disease. Likewise, the CDC strains and the local strains were isolated with equal frequency.

This work shows that some culture media are unable to support growth of low inoculums of Neisseria gonorrhoeae. Unless the blood culture media used is known to support the rapid growth of small numbers of Neisseria gonorrhoeae, multiple different media should be used to obtain blood cultures in suspected cases of Neisseria gonorrhoeae sepsis.

Status: Completed.

Potts, D.W., Stevens, D.L, and McNitt, T.R. Disseminated Neisseria gonorrhoeae. Submitted to British Journal of Venereal Disease.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Antidiar, Lomotil and Placebo in Acute Diarrhea.

WORK UNIT NO.: C-9-79

PRINCIPAL INVESTIGATOR: LTC Ernest L. Sutton

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effectiveness of Antidiar^R, an over-the-counter drug; of Lomotil^R, a prescription drug approved as effective adjunctive therapy; and of a placebo in the treatment of acute diarrhea.

TECHNICAL APPROACH

Patients age 18-65 presenting to the Brooke Army Medical Center Troop Clinic, Emergency Room and Acute Minor Illness Clinic with symptoms compatible with a diagnosis of acute diarrhea, will be considered for this study. The diarrhea must have begun less than 48 hours before enrollment in the study, and the patient must have experienced at least three watery, liquid or loose bowel movement within the previous twenty-four hours. Eligible participants will be assigned to one of three groups. Group I will receive Antidiar, Group 2 will receive Lomotil, and Group III will receive the Antidiar vehicle.

Personnel: None.

Funding: None.

PROGRESS

Thirty-eight patients have completed the study. Results are not available at this time.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Plasmapheresis in Treatment of Hypereosinophilia Syndrome
Associated with Recurrent Staphylococcal Skin Abscesses.

WORK UNIT NO.: C-10-79

PRINCIPAL INVESTIGATOR: Larry D. Hudson, M.D., CPT, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To decrease levels of circulating IgE and other serum factors which may contribute to abnormal polymorphonuclear chemotaxis and phagocytosis, eosinophilia, anergy, and severe pruritus.

TECHNICAL APPROACH

Patients with staph abscess, hypereosinophilia, anergy, severe pruritus and hyper IgE will undergo plasmapheresis in an attempt to induce a remission.

Personnel: None.

Funding: None.

PROGRESS

One patient was entered on the study, and the results were equivocal. Due to the rarity of the syndrome, it was decided to discontinue the study.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Headache and Back Pain Clinical Algorithm Validation, Cost Analysis, and AMOSIST Reliability.

WORK UNIT NO.: C-13-79

PRINCIPAL INVESTIGATOR: Robert D. Slay, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: N. Joe Thompson, M.D., LTC, MC; Robert E. Jackson, III, M.D., LTC, MC; Stanley Harris, M.D.; Barry W. Wolcott, M.D., LTC, MC; Bob Woods, M.D.; Larry E. Slay, M.D., LTC, MC

OBJECTIVES

1. To determine if new clinical algorithms, used to evaluate and treat patients presenting with acute headache and back pain, utilized by physician extenders, can be validated as effective in an outpatient population.
2. To compare the process of outcome data obtained by AMOSISTS and Internists (utilizing the same standard data base) in the evaluation and treatment of adults with headache or back pain.
3. To utilize the process of outcome data generated by the AMOSISTS and Internists to generate new clinical algorithms of measurable cost and outcome.

TECHNICAL APPROACH

Patients are screened selectively for headache and back pain using our standard triage manual. They are then seen by either an AMOSIST or staff internist, who complete a standardized data collection sheet. The outcomes of treatment provided by both care providers is assessed and compared. A retrospective chart review is done by an independent internist and a diagnosis is established.

Personnel: None.

Funding: None.

PROGRESS

To date, approximately 952 patients have been entered into the study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Immunoglobulin Regulation in Rheumatic Disease.

WORK UNIT NO.: C-14-79

PRINCIPAL INVESTIGATOR: Stephen J. Van Cleave, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To further characterize the physicochemical properties of amplifier factor in patients with systemic lupus erythematosus, rheumatoid arthritis, dermatopolymyositis, progressive systemic sclerosis, Sjogren's syndrome and sarcoidosis, and to study the cellular interactions responsible for its function.

TECHNICAL APPROACH

This is a collaborative study with Dr. I. Jon Russell, University of Texas Health Science Center at San Antonio.

Blood samples will be obtained from normal control volunteers and from patients with a variety of connective tissue diseases including systemic lupus erythematosus, rheumatoid arthritis, dermatopolymyositis, progressive systemic sclerosis, Sjogren's syndrome and sarcoidosis for evaluation as outlined in the study protocol.

Personnel:

Funding: None.

PROGRESS

To date, no patients from BAMC have been entered on this study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Neutrophil Chemotaxis and Phagocytic Activity in Psoriasis Vulgaris.

WORK UNIT NO.: C-17-79

PRINCIPAL INVESTIGATORS: Charles S. Fulk, M.D., MAJ, MC; Robert C. Allen, M.D., Ph.D., CPT, MC

ASSOCIATE INVESTIGATORS: Deborah Hunter, SP5

OBJECTIVES

To research the functional dynamics of neutrophil chemotaxis and phagocytic activity in psoriasis vulgaris patients as compared to psoriatics undergoing treatment with 8-methoxypsoralen and ultraviolet light (PUVA) and nonpsoriatic controls.

TECHNICAL APPROACH

Polymorphonuclear leukocytes from untreated psoriatics are examined for chemiluminescence as a function of oxidative metabolism in response to known stimulants and psoriatic stratum corneum scale. Psoriatic stratum corneum scale is homogenized and an extract is prepared. Chemotaxis of polymorphonuclear leukocytes to this extract by an under agarose technique is performed.

Personnel: 1 SP5 (3 months)

Funding: FY 79

Consumable Supplies \$3,038.00

PROGRESS

To date, ten patients have been included in the study. The oxidative microbicidal response of the patient's cells when compared with normal controls did not indicate a defect in polymorphonuclear leukocyte metabolic response.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Controlled Clinical Trial Comparing the Efficacy and Safety of Amcinonide (0.1% Cream) with Betamethasone Valerate (0.1% Cream) in Patients with Psoriasis.

WORK UNIT NO.: C-21-79

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Assessment of the efficacy and safety of amcinonide (0.1% cream) as compared with betamethasone valerate (0.1% cream) in the treatment of psoriasis without the use of occlusive dressings.

TECHNICAL APPROACH

This is a double blind clinical trial comparing amcinonide cream to valisone cream.

Personnel:

Funding:

PROGRESS

To date, eighteen patients have been included in the study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Peripheral Neuropathy - A Complication of Cis-Dichloro-
diammine Platinum - II (NSC - 119875).

WORK UNIT NO.: C-22-79

PRINCIPAL INVESTIGATOR: J. D. Cowan, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: M. S. Kies, M.D., MAJ, MC; R. Joyce, M.D.;
J. Roth, M.D., COL. MC

OBJECTIVES

1. To determine the incidence of peripheral nerve damage after Cis-Dichlorodiammine Platinum II (C-DDP) therapy.
2. To quantify peripheral nerve damage by motor and sensory nerve conduction analysis.

TECHNICAL APPROACH

Eleven solid tumor patients were treated with C-DDP as a single agent at Brooke Army Medical Center. All were invited to participate in this study.

Prior to the first C-DDP exposure, all patients underwent a neurologic history and physical examination and a battery of laboratory tests including a CBC, serum calcium, fasting and two hour postprandial blood sugar, VDRL, thyroid function tests, serum folate level, serum B-12 level, ANA, rheumatoid factor, urinalysis, and 24-hour urine screen for heavy metals; and nerve conduction studies of the right upper and lower extremities consisting of distal motor latency, distal sensory latency, forearm motor nerve conduction velocity of the ulnar and median nerves, distal motor latency and leg motor nerve conduction velocity of the peroneal nerve, and leg sensory nerve conduction velocity of the sural nerve. Prior to each subsequent dose of C-DDP and 2-6 weeks after the last dose of C-DDP, a repeat history, physical examination and nerve conduction studies were performed. The nerve conduction studies were considered consistent with a peripheral neuropathy if at least 50% of the measurements were greater than one standard deviation from the norm.

Personnel: None.

Funding: None.

PROGRESS

Eight of the eleven patients treated with C-DDP as a single agent were evaluable. Two patients were excluded because of early death due to their primary tumor, and one patient was excluded due to loss of follow-up. There were seven men and one woman with four patients having epidermoid lung cancer, three having squamous cell carcinoma of the head and neck, and one ovarian cancer.

The pretreatment history and physical examinations were negative in six of eight patients. One patient had a bilateral lower extremity muscle weakness due to pain from femoral bone metastases, and one patient had bilateral decreased vibratory sense in the lower extremities. The laboratory screen was negative for all eight patients. Although seven of eight patients had an abnormal ulnar forearm nerve conduction velocity and five of eight patients had a slowed sural nerve conduction velocity prior to treatment with C-DDP, only two patients had a pretreatment pattern of a peripheral neuropathy.

The history and physical examination after completion of all C-DDP treatment revealed no new clinical peripheral neuropathies. The nerve conduction studies after completion of all C-DDP did not demonstrate the development of subclinical peripheral neuropathies.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Triple Corticoid Integrated System (TCIS) 0.015% Cream Compared to 0.5% Hydrocortisone Cream in Treating Lichen Planus.

WORK UNIT NO.: C-34-79

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the efficacy of TCIS cream (0.015%) in lichen planus without occlusion,
2. To compare the efficacy of TCIS cream (0.015%) against 0.5% hydrocortisone in the same vehicle in treating lichen planus.

TECHNICAL APPROACH

This study will be conducted as outlined in the drug company protocol.

Personnel: None.

Funding: None.

PROGRESS

This project has not been started.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Maintenance of Patency of the Ductus Arteriosus in Neonates with Cyanotic Congenital Heart Disease.

WORK UNIT NO.: C-35-79

PRINCIPAL INVESTIGATOR: Kenneth R. Bloom, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Joseph P. Murgo, M.D., LTC, MC

OBJECTIVES

To maintain an adequately patent ductus arteriosus in neonates who have cardiac malformations such that their immediate survival is dependent on blood flow through this channel. This will be done by infusion of Prostaglandin E₁ until diagnostic studies are completed and surgery carried out.

TECHNICAL APPROACH

Newborn infants presenting to the neonatal intensive care unit at BAMC and who have cyanotic congenital heart disease form this study group. Prostaglandin is infused either through an umbilical artery catheter placed at the level of the ductus or, in some conditions, intravenously. Effects of the prostaglandin infusion are assessed by peripheral PO₂ measurement and, when applicable, by blood pressure measurements in the leg.

Personnel: None.

Funding: None.

PROGRESS

To date, two patients have been treated. One had Tetralogy of Fallot with pulmonary atresia and one had hypoplastic right heart syndrome. Both showed marked improvement once prostaglandin (PGE) infusion was started. The PO₂ improved by 100% in each. One child had surgery, the surgical procedure was ineffective, and PGE was restarted and the child kept alive until a second operation could be done. The other child was maintained in good condition and survived palliative surgery.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Stability of Cytarabine in Bicarbonate Infusion Solutions.

WORK UNIT NO.: C-36-79

PRINCIPAL INVESTIGATOR: Bruce R. Harrison, CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVE

To ascertain the stability of cytarabine in normal infusion solutions containing sodium bicarbonate.

TECHNICAL APPROACH

Clinical concentrations of cytarabine in D5W with and without NaHCO_3 added are being scanned to determine the maximum absorbance. An analysis of the loss of absorbance when exposed to high pH will reflect the concentration of drug remaining over selected time intervals.

Changes in UV absorbance in the described solutions of cytarabine will be determined using spectrophotometry.

Personnel: None.

Funding: None.

PROGRESS

The pH range of the various test solutions has been determined. Familiarization with the spectrophotometer has been completed and trial scans of absorbance vs. wavelength have been completed. The OD_{max} has been determined and compared to published data.

Proper dilution of the test solutions has been a problem and is being tested.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ankle Trauma Study

WORK UNIT NO.: C-37-79

PRINCIPAL INVESTIGATOR: N. Joe Thompson, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Robert Highley, M.D.; James Bushyhead, M.D.;
Barry Wolcott, M.D., LTC, MC; Robert Wood, M.D.

OBJECTIVES

1. To define predictors for the clinical diagnosis of ankle fracture, ligament rupture and ligament strain.
2. To develop a cost efficient scheme for x-ray utilization in the diagnosis of ankle trauma.
3. To evaluate the effects of different treatment modalities, including "soft cast" dressing and plaster casts for varying periods of time on ultimate outcome following ligamentous ankle sprains.
4. To elucidate the natural history of ankle trauma based on the denominators with all those seeking primary care for their ankle trauma. This includes the natural history of ankle pain, swelling, ecchymosis, etc. as well as the quantification of the subsets of trauma, i.e. number of fractures, avulsions, sprains or ligament ruptures seen in this population.
5. To construct a family of algorithms, each with its specific cost efficiency ratios.
6. To determine the best protocol for optimum quality of care in ankle trauma.

TECHNICAL APPROACH

All patients with inversion injuries of the ankle, i.e. sprains, ruptures, avulsions, fractures and fractures of long bones will be the main subject of the proposed study. History and physical checklist will be completed by a study doctor and a prediction made of the likelihood of the following diagnosis: (1) fracture - avulsion; (2) rupture (ligament or tendon); or (3) sprain. After the prediction is recorded, AP, lateral and mortise plain films of the ankle are done.

C-37-79 (Continued)

After x-ray results have been obtained, the primary doctor separates the patients with fractures from those with non-fractures. The patients with fractures are referred to the Orthopedic Service, and all major fractures are removed from the study. The doctor then repredicts the likelihood of: (1) fracture; (2) rupture (tendon or ligament); or (3) sprain on those patients not shown to have a fractures by the plain films.

Personnel: None.

Funding: None.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Inhibition of Premature Labor with Terbutaline.

WORK UNIT NO.: C-39-77

PRINCIPAL INVESTIGATOR: Charles H. Burton, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Alexander G. Juden, Jr., M.D., COL, MC;
Milton H. Leman, M.D., LTC, MC

OBJECTIVES

To study the inhibitory effects of terbutaline on premature labor.

TECHNICAL APPROACH

Patients of less than 36 weeks gestation admitted to the Obstetric Service in premature labor will be initially treated with terbutaline. Terbutaline will be administered by an initial intravenous loading dose, followed by a subcutaneous dose for 24 hours, followed by a p.o. maintenance dose. During the p.o. maintenance, one-half of the patients will receive an oral placebo and one-half of the patients will receive oral terbutaline.

Personnel: None.

Funding: None.

PROGRESS

This protocol was suspended by direction of the FDA pending toxicology studies.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prolactin Levels in Hypertensive Pregnancies.

WORK UNIT NO.: C-8-78

PRINCIPAL INVESTIGATOR: Joseph C. Webster, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Alexander G. Juden, Jr., M.D., COL, MC;
Residents, Department of Obstetrics and
Gynecology

OBJECTIVES

To determine whether hypertension occurring after onset of pregnancy is associated with elevated prolactin levels as compared with normotensive pregnancies.

TECHNICAL APPROACH

Serum prolactins are being drawn at certain stages in gestation prior to 1030 hours to avoid diurnal changes. The values present in those eventually becoming pre-eclamptic will be compared with values from normotensive patients.

Personnel: None.

Funding: None.

PROGRESS

The laboratory service could not support the number of prolactin assays required. Therefore, the study was terminated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Comparison Study of Cesarean Section.

WORK UNIT NO.: C-39-78

PRINCIPAL INVESTIGATOR: Danny R. Barnhill, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: David L. Caldwell, M.D., CPT, MC; Roger L. Wallace, M.D., CPT, MC; Alexander G. Juden, Jr., M.D., COL, MC

OBJECTIVES

To determine if postoperative Cesarean section febrile morbidity can be reduced by operative technique or prophylactic antibiotics.

TECHNICAL APPROACH

This study was designed to determine if the high postoperative infectious morbidity (37%) associated with primary cesarean sections could be altered by either using prophylactic antibiotics or the technique of extraperitoneal cesarean section. Early in the study it was found that the incidence of wound infections was significantly increased in extraperitoneal cesarean sections unless subfascial drains were employed. Since this type of drainage is a standard surgical technique, it has now been added to the extraperitoneal cesarean sections.

Personnel: None.

Funding: None.

PROGRESS

Since the great majority of primary cesarean sections are done by first year residents, there has been a natural reluctance to have them perform extraperitoneal cesarean sections until the current "standard" transperitoneal technique has been mastered. Because of this, through April 1979 there had been 24 extraperitoneal cesarean sections in the study with an infection rate of 20%. The prophylactic antibiotic group is somewhat larger and is still being tabulated,

C-39-78 (Continued)

but it appears that this group is also going to have a significantly lower infection rate of about 20%. Although the progress has been slower than initially anticipated, the preliminary results are encouraging.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Terbutaline Sulfate as an Adjunct to the Management of Intrapartum Fetal Distress.

WORK UNIT NO.: C-1-79

PRINCIPAL INVESTIGATOR: Robert M. Young, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: George E. Matthews, D.O., CPT, MC; Alexander G. Juden, Jr., M.D., COL, MC

OBJECTIVES

To evaluate the efficacy of Terbutaline Sulfate in the management of acute intrapartum fetal distress, either as a resuscitative modality or as a temporizing measure in preparation for delivery of the distressed fetus.

TECHNICAL APPROACH

Patients manifesting persistent intrapartum fetal distress in the first stage of labor as evidenced by FHR deceleration patterns and/or fetal scalp pH criteria will be participants in the evaluation of Terbutaline Sulfate as a resuscitative or temporizing measure.

Personnel: None.

Funding: None.

PROGRESS

This protocol was never activated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Uterine Exteriorization at Cesarean Section.

WORK UNIT NO.: C-11-79

PRINCIPAL INVESTIGATORS: Joseph C. Webster, M.D., CPT, MC; Danny R. Barnhill, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Alexander G. Juden, Jr., M.D., COL, MC

OBJECTIVES

To determine whether the postoperative morbidity associated with intra-operative exteriorization of the uterus at cesarean section differs significantly from patients whose uteri remain intra-abdominal at cesarean section.

TECHNICAL APPROACH

Only patients scheduled for elective repeat cesarean sections, at term, not in labor, with intact membranes and afebrile will be included in the study. Standard preoperative and postoperative care, surgical technique, and anesthesia will not be altered for the study. The only variable will be exteriorization or non-exteriorization of the uterus which will be determined by random card selection.

Personnel: None.

Funding: None.

PROGRESS

This protocol was never activated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinicopathologic Study of Uterine Vascular Changes with and without Hormonal Influence.

WORK UNIT NO.: C-12-79

PRINCIPAL INVESTIGATOR: Charles V. Wilson, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Alexander G. Juden, Jr., M.D., COL, MC;
Milton H. Leman, M.D., LTC, MC

OBJECTIVES

To study the association of intimal thickening of uterine arteries with oral contraceptive use in women undergoing hysterectomy with, and without cervical and uterine pathology.

TECHNICAL APPROACH

All patients undergoing hysterectomy, for whatever reason, by an abdominal or vaginal route, will be eligible for the study. The operative specimen will be taken directly by the pathologist for both electron microscopic and light microscopic fixation and preparation. Sections will be made of both uterine and myometrial vessels and examined for intimal thickening and other abnormal vascular changes. The patients will be divided into study groups for comparison as follows: Group I - no hormonal exposure; and Group II - hormonal exposure, 50-100 micrograms, for 1 year, 1-2 years, or 2 years or more.

Personnel: None.

Funding: None.

PROGRESS

This project will start in the near future.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Diagnosis and Management of Hemostatic Changes in Cardiac
By-Pass Surgery.

WORK UNIT NO. C-17-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard C. Traugott, M.D., LTC, MC; Special
Hematology Staff

OBJECTIVES

To determine the specific hemostatic changes occurring during cardiac
by-pass surgery.

TECHNICAL APPROACH

A battery of hemostatic tests will be performed on all scheduled cardiac
by-pass surgery patients within three days before surgery. These in-
clude: Protime (PT), activated partial thromboplastin time (APTT),
bleeding time (BT), platelet count (PC), split products (FSPs), thrombin
time (TT), fibrinogen (I), factor IX assay, factor VIII assay, reptilase
time (RT) if the TT is abnormal), platelet aggregation, and platelet
adhesivity (Wright).

Coagulation results for each patient will be correlated with the
patient's clinical status and interpreted by standard techniques.
When abnormalities are delineated, appropriate corrective action will
be undertaken. Abnormalities noted will be tabulated for the entire
series and correlated with patient's age, status, operation, opera-
tion time, pump time, heparin dose, protamine dose, blood loss, blood
product replacement and unusual operative complications.

Personnel: None

Funding: None

PROGRESS

Approximately 500 patients have been studied. There have been no
major new discoveries not previously described. There has been an

C-17-77 (Continued)

improvement in the coag-hemostasis and blood-blood products management of these patients, in part due to the programmed, regular, extensive evaluation of the patients. This study will continue as routine patient management.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Laser Nephelometric Assay of Factor VIII Antigen and Anti-Thrombin III (AT-III).

WORK UNIT NO.: C-25-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Agnes Rohan, DAC, Brenda Harris, DAC, Madelyn Stewart, DAC; Dan Marmer, DAC; John Posch, DAC

OBJECTIVES

To establish a rapid immunologic assay of factor VIII Antigen and AT-III using a laser nephelometer.

TECHNICAL APPROACH

When a satisfactory system is developed, AT-III will be determined in a series of normal and abnormal patients by the nephelometric procedure and by radioimmunodiffusion. Results of the two methods will be compared by linear regression analysis.

Factor VIII determinations will be performed by nephelometry and by electroimmunodiffusion for a series of normal and deficient patients. Nephelometric results will be compared with EID results by linear regression analysis.

Personnel: None.

Funding: None.

PROGRESS

Studies were undertaken using an animal antibody to Factor VIII and a variety of buffering solutions. Initial efforts were promising; however, due to lack of technical help, the study was abandoned.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hemoglobinopathy Testing of United States Army Inductees -
Analysis of Two Systems.

WORK UNIT NO.: C-44-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: V. Coley, MAJ, MSC; Agnes Rohan, DAC, Madelyn
Stewart, DAC; Brenda Harris, DAC; John Posch,
DAC; Dan Marmer, DAC

OBJECTIVES

To analyze the cost per subject, error rate, feasibility for mass screening and rate of detection of abnormal hemoglobin variants with two screening systems, one based on a semiautomated dithionate screen for sickle hemoglobin and the second based on a Coulter S CBC and cellulose acetate hemoglobin electrophoresis.

TECHNICAL APPROACH

A pilot study will be conducted testing 5,000 student volunteers at the Academy of Health Sciences using two testing systems:

- a. Semiautomated dithionate testing, with confirmation of abnormals by cellulose acetate hemoglobin electrophoresis.
- b. Coulter S CBC with reticulocyte count and cellulose acetate hemoglobin electrophoresis with densitometric A₂ quantitation, alkali denaturation hemoglobin F determine, and clarification of borderline A₂ values by column chromatography. Abnormal results will be investigated and confirmed by standard laboratory methods.

Personnel: None

Funding: None

PROGRESS

One hundred and twenty-six volunteers were studied in a pilot study. Four cases of AS were identified by both systems, and two cases of AC by the latter system. No other abnormalities were found. This study resulted in a more rational approach to testing of inductees.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: a. Compilation of Atlas of Electron Micrographs of Known Viruses.
b. Electron Microscopic Examination of Selected Viral Cultures
for Detection of Mixed Viral Infections.

WORK UNIT NO.: C-45-77

PRINCIPAL INVESTIGATOR: George J. Kasai, Ph.D.

ASSOCIATE INVESTIGATORS: Thomas Perez, DAC; Steven K. Koester, DAC; Lucy
Olalde, DAC; Lt Knight and Lt Brian Kiehl, USAR

OBJECTIVES

Additional micrographs will be collected to add to those already on file. The micrographs will be used to compare with unknown forms as an aid to further identification. Ultra structures will be studied so that groupings can be made on such findings. Studies of possible mixed viral infections will be continued although from our past experiences this appears to be a rather difficult task. Our first success along these objectives appears to have resulted by accident.

TECHNICAL APPROACH

We will continue to study those cytopathic effects in tissue culture that do not lend themselves to neutralization with our present bank of antisera. We have added another dimension to this study with the introduction of the hematoxylin eosin (H&E) stain technique of Dr. Melherbie. This H&E stain technique allows us to view the inclusion bodies and to place the viral agent into definitive groups. Another technique resorted to is that of negative staining of viruses - a procedure introduced into this laboratory by LT Brian Kiehl from the University of West Florida. Collection of electron micrographs will be continued and correlations will be attempted with the other methods described above.

Personnel: None.

Funding: None.

PROGRESS

Negative staining procedures have been reported as being useful for rapid viral identification. The technical aspects of this procedure need further study to allow for the proper concentration and cleaning-up of the

C-45-77 (Continued)

sample. Preliminary studies have been very encouraging with the proper identification of an adenovirus and a picorna virus. Both specimens were difficult to identify by the neutralization method until further titrations and quantitations on the antisera had initially been done. Although the study is anticipated to continue, it will progress with the availability of time.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hemoglobinopathy Testing of United States Army Inductees -
Natural History of Hemoglobinopathies in the Army.

WORK UNIT NO.: C-48-77

PRINCIPAL INVESTIGATOR: David R. Head, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To prospectively identify and follow individuals with hemoglobinopathies and matched controls for morbidity in an Army Environment.

TECHNICAL APPROACH

Individuals with hemoglobinopathies identified in Part A (C-44-77) of this project will be informed of genetic implications and possible morbidity of their hemoglobinopathy and/or hematologic abnormality. They will be paired with normal (AA) individuals, and after assignment will be followed for a minimum of two years with CBC and reticulocyte count every six months. Participants will remain in the study until discharged from the Army, or termination of the study.

Personnel: None.

Funding: None.

PROGRESS

This study was not done.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparative Survey of Ruba-Cell and Ruba-Tec Procedures on Submitted Specimens. Evaluation of the ELISA Method for Rubella Screening in a Clinical Diagnostic Laboratory.

WORK UNIT NO.: C-3-78

PRINCIPAL INVESTIGATOR: George J. Kasai, Ph.D.

ASSOCIATE INVESTIGATORS: Bonita A. Dooley, DAC; Sheryl Talley, DAC;
Joyce Goodrich, E-5; Rick Garis, E-6

OBJECTIVES

Rubella screening was carried out by various procedures to determine which would be the best and most economical method to be used in the laboratory.

TECHNICAL APPROACH

Both the Ruba-Cell and Ruba-Tec kits were compared on several hundred patient specimens with hi-pos, lo-pos and negative controls. These were then compared with results obtained using the International Diagnostic Technology's FIAX procedure which is a fluorescent method. The ELISA procedure which was available on the domestic market was unstable due to the deterioration of the enzyme conjugate. The results were submitted to the OB-GYN clinic for evaluation.

Personnel: None.

Funding: None.

PROGRESS

This screening procedure was terminated because the decision was made to use the IDT-FIAX procedure for all future reporting of rubella serum titers. The Ruba-Cell procedure was to be used as a back-up procedure as it was a qualitative test and did not determine titers. Additional suggestion is offered to investigate the Gilford Instrument's Automated EIA procedure for rubella. At the present time this test procedure is being developed but the preliminary reports indicate that the test is as sensitive as the IDT-FIAX procedure and is also quantitative.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234

INVESTIGATION PROJECT RESUME

TITLE: Oxauracil Typing of Herpesvirus simplex Type I and II Clinical Isolates

WORK UNIT NO.: C-33-78

PRINCIPAL INVESTIGATOR: Lawton A. Seal, 1LT, MSC

ASSOCIATE INVESTIGATORS: Steven K. Koester, DAC; Richard M. Jamison, Ph.D.

OBJECTIVES

1. To evaluate the efficacy of Oxauracil in the differentiation of HSV clinical isolates (wild strains) using tissue culture cell lines currently available in the Virology Laboratory.
2. To establish a new and rapid procedure for typing HSV wild strains, thereby reducing the time required to obtain reliable results.

TECHNICAL APPROACH

The purpose of this study was to compare the efficiency of Oxauracil with specific antiserum neutralization and fluorescent antibody staining techniques in the typing of clinical isolates of HSV. Thirty clinical isolates of HSV were types (as to HSV-I or HSV-II) by the methods stated above in several tissue culture cell lines.

Personnel: None.

<u>Funding:</u>	FY 79	FY 78
Consumable Supplies	\$260.00	\$312.92

PROGRESS

The data have been compiled and results analyzed. The results indicate Oxauracil to be a very accurate method (as determined by Chi-square analysis) for HSV typing in primary rabbit kidney cells (RKC) and a continuous RKC line. Attempts at typing in other cell lines were not successful. In addition to accuracy equal to or greater than the other methods employed, the Oxauracil technique is easy to perform and offers results in 24 hours.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Use of Hamsters in Experimental Studies in Amebiasis.

WORK UNIT NO.: C-18-79

PRINCIPAL INVESTIGATOR: Roy G. Taylor, Ph.D., MAJ, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the effects of Entamoeba histolytica and cyclophosphamide in the hamster model of hepatic amebiasis.

TECHNICAL APPROACH

Animals will be anesthetized with sodium pentobarbitol given intraperitoneally. A midline incision will be made and the portal vein exposed. The dose of amebae will be introduced through a 26 gauge needle on a tuberculin syringe. Ten animals in two groups will be infected with HM-1:IMSS. One group will receive cyclophosphamide 24 hours prior to infection in a dose of 225 mg/kg body weight, and the drug will be administered intraperitoneally.

Personnel: None.

Funding: None.

PROGRESS

The principal investigator was transferred to WRAIR before any meaningful results were obtained.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Morbidity and Mortality Induced in Suckling Swiss Mice by Oxauracil.

WORK UNIT NO.: C-23-79

PRINCIPAL INVESTIGATOR: Lawton A. Seal, 1LT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the morbidity and mortality induced by the pyrimidine analog Oxauracil in suckling mice.

TECHNICAL APPROACH

Sixty suckling mice were divided randomly into six groups and treated, as outlined in the protocol, with saline or various concentrations of Oxauracil by daily I.P. injections.

Personnel: None.

Funding: None.

PROGRESS

Although there was no increase in the mortality of the animals receiving higher concentrations of the drug (10^{-2} m Oxauracil and greater daily dosages), alopecia was observed on the ventral surface surrounding the injection sites of those animals receiving drug concentrations greater than 10^{-3} m. Linear regression analysis indicates a strong inverse relationship ($r = -.95$, $p < 0.02$) exists between the drug dosage administered and the leukocyte count. As the drug concentrations increased, the leukocyte count declined to well below the limits of

C-23-79 (Continued)

normal, thereby indicating a drug induced leukopenia. Only animals receiving 0.2 ml of 10^{-3} m Oxauracil in daily injections maintained normal leukocyte counts. It was concluded, therefore, that 10^{-3} m Oxauracil in daily I.P. injections was the treatment regimen of choice, as no drug toxicity was ascertainable in animals so treated.

Status: Completed.

Seal, L.A. Evaluation of the effectiveness of 2H-1,3 Oxazine-2,y(3H)-dione (Oxauracil) in the treatment of Herpesvirus simplex (HSV) induced acute encephalitis in mice. Submitted to Antimicrobial Agents and Chemotherapy for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Pediatric Clinical Algorithm Validation, Cost Analysis and PAMOSIST Reliability.

WORK UNIT NO.: C-2-78

PRINCIPAL INVESTIGATOR: Frank P. Wilson, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if a pediatric clinical algorithm utilized by physician extenders can be validated in a pediatric outpatient population.
2. To compare the process and outcome data obtained by PAMOSIST's and pediatricians utilizing a standardized data base in the evaluation and treatment of children with acute URI complaints.
3. To utilize the process and outcome data generated by PAMOSIST's and pediatricians to generate clinical algorithms of measurable cost and outcome.

TECHNICAL APPROACH

Complete medical history and physical examination data were collected on a checklist which was transcribed and programmed into computer terminals at USPHS, Seattle, Washington. Data compiled was then analyzed as to PAMOSIST error in both algorithm usage and treatment protocols received.

Personnel: None.

Funding: None.

PROGRESS

Nonprofessionals utilizing physician-written triage algorithms were used to assign the care urgency category of 2,000 walk-in pediatric patients. Algorithm-directed nonprofessionals agreed with the physician's classification of urgency needs (made after evaluation of the patient), in 84% of cases. The screener assigned a higher care urgency classification in 15% of cases and a lower classification in only 1.2% of cases. No patient danger resulted from the algorithm-directed screening of pediatric patients.

Status: Completed.

C-2-78 (Continued)

Wilson, F.P., Jr., Wilson, L.O., Butler, A.B., and Canales, L. Pediatric algorithm-directed triage: a prospective study. Submitted to JAMA for publication.

Wilson, L.O., Wilson, F.P., Jr. and Canales, L. Algorithm-directed triage in pediatrics: a safe system that facilitates the study and planning of non-appointed health care. Submitted to JAMA for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of Cisternography Utilizing ¹¹¹Indium DTPA.

WORK UNIT NO.: C-35-74

PRINCIPAL INVESTIGATOR: Robert Telepak, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Roswell Beck, M.D., MAJ, MC

OBJECTIVES

To evaluate the safety and efficacy of ¹¹¹Indium DTPA for cisternography.

TECHNICAL APPROACH

Cisternograms using ¹¹¹In DTPA are being done to diagnose subarachnoid blocks, presence of abnormal CSF circulation (especially backward flow into the lateral ventricles as seen in communicating hydrocephalus), and CSF leaks such as rhinorrhea or otorrhea. The radionuclide is introduced intrathecally via an LP and then images performed at approximately 6, 24 and even at 48 hours later. Cotton pledgets in the nostrils and ears are inserted and counted to check for CSF leakage in appropriate cases.

Personnel: None.

Funding: None.

PROGRESS

Nine cases have been done during 1979 and have yielded very useful clinical and diagnostic information about the patients.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Intravenous Administration of ¹³¹I-6-B-Indomethylnorcholesterol
(NP-59) for Adrenal Evaluation and Imaging.

WORK UNIT NO.: C-12-77

PRINCIPAL INVESTIGATOR: Robert Telepak, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Roswell Beck, M.D., MAJ, MC

OBJECTIVES

Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenal-cortical disorders and as a potential scanning agent for detecting structural abnormalities of the adrenal medulla.

TECHNICAL APPROACH

The radiopharmaceutical is injected IV and then the patient is scanned first at 3-4 days and again at about 7-10 days. Dexamethasone suppression is sometimes employed in conjunction with the scan to check for evidence or lack of suppression. An attempt is made to evaluate the percent uptake of the NP-59 by each of the adrenal glands to differentiate bilateral hyperplasia (Cushing's disease) from unilateral disease (adrenal cortical adenoma). Secondary information can be gained about adrenal medullary tumors such as pheochromocytoma. Other cortical problems such as hyperaldosteronism and androgen-excess syndromes can also be evaluated.

Personnel: None.

Funding: None.

PROGRESS

Two patients have been scanned so far in 1979 with useful diagnostic results (1 bilateral hyperplasia and 1 adenoma diagnosed).

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Technetium-99m-pyridoxylideneglutamate (99m-Tc-PG) for Diagnosis of Hepatobiliary Disease.

WORK UNIT NO.: C-22-78

PRINCIPAL INVESTIGATOR: Robert Telepak, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Roswell Beck, M.D., MAJ, MC

OBJECTIVES

To evaluate the clinical efficacy of Tc-99m-PG as a diagnostic hepatobiliary and gallbladder agent.

TECHNICAL APPROACH

IV injection of the radiopharmaceutical is employed followed by sequential imaging of the anterior abdomen. The time of appearance of liver visualization, common bile duct, cystic duct, gallbladder, and evidence of activity in the bowel are all assessed. This procedure has been very helpful in differentiating normal, acute cholecystitis, chronic cholecystitis, partial biliary obstruction, and total biliary obstruction. It is fast, safe, and much more useful for evaluation of the biliary system than the OCG or OVC in cases of elevated total bilirubin. It is now a part of the routine diagnostic approach of such patients along with ultrasound, ERCP, and transhepatic cholangiography.

Personnel: None.

Funding: None.

PROGRESS

Twenty-two cases have been done so far in 1979 and have been very useful in providing good diagnostic information on the patients in whom it was performed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comprehensive Rehabilitation of the Laryngectomee.
(Collaborative Study with the University of Texas at San Antonio)

WORK UNIT NO.: C-21-76

PRINCIPAL INVESTIGATOR: Sonley R. LeMay, Jr., M.D., COL, MC

ASSOCIATE INVESTIGATORS: George A. Gates, M.D.; Edmund Lauder, M.S.;
J. C. Cooper, Ph.D.

OBJECTIVES

To acquire normative data about the biological, psychological, social and employment aspects of laryngectomee rehabilitation; to demonstrate a comprehensive program of rehabilitation is more efficient than current methods; and to statistically validate the indices of successful and unsuccessful rehabilitation.

TECHNICAL APPROACH

Preoperatively, written informed patient consent is secured. Biological, biographical, psychological, social, employment and financial data are obtained. Speech data and a brief interview are recorded on videotape. Each patient is presented with standardized educational material and a criterion based test.

Postoperatively, a second auditory evaluation is made. A treatment plan is developed based on the patient's physical condition and psychological and speech evaluations. One to two hour individual and/or group speech therapy sessions are conducted weekly. Progress is assessed monthly. Three and six month follow-up evaluations are performed with respect to esophageal speech fluency and technical proficiency, psychological and social adjustment, and employment and financial status. Manometric data are again obtained at the end of six months.

Retrospective control patients undergo comparable assessment procedures as detailed in the grant proposal.

Personnel: None

Funding: None

PROGRESS

Evaluation of the data obtained from this study is not completed. However, it has been determined that 36/48 study subjects attempted to learn esophageal speech. Of these, nine used esophageal speech (ES) only and three others used esophageal speech and the electrolarynx (EL) as their dominant mode of communication. The success rate for acquisition of ES was 12/36 (33%). Of the 24 who were not successful in learning ES, eight used the EL, and the others used manual communication. The twelve patients who did not attempt to learn ES used the EL primarily (8) or wrote (4).

All patients were offered instruction in esophageal speech and electrolarynx use. The study subjects received an average of 5.3 months of speech therapy (range 1-6 months) consisting of 12.5 lessons. The majority (57%) used an electrolarynx for communication during the period of time they were learning or attempting to learn esophageal speech. Women received significantly more months of speech therapy than did men, and the total number of lessons differed significantly between institutions.

In evaluating the psychosocial effects of laryngectomy the following was found: (1) Denial - almost one-half of the subjects exhibited substantial denial; (2) Self-Image - the majority had a poorer image of themselves after laryngectomy; (3) Attitude Toward Life - the majority had a poorer attitude towards life (57%) but 41% felt the same as before their illness; (4) Social Life - 59% indicated that their social activities were substantially reduced; 41% indicated that no change had occurred.

With reference to employment, the majority of patients returned to their pre-illness situation - the same job, a comparable job, or retirement.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Determination of Preventive Keflin Delivered to the Site of
Total Joint Replacement.

WORK UNIT NO.: C-22-77

PRINCIPAL INVESTIGATOR: Thomas J. Parr, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Neal A. Jewell, M.D.

OBJECTIVES

To determine the levels of cephalosporin delivered to the site of total joint replacement procedures: 1) To determine an exact dose/route regimen in total joint replacement; 2) to thereby devise a standardized protocol for preoperative, intraoperative and postoperative administration of preventive antibiotic in total joint replacements.

TECHNICAL APPROACH

Patients in this study have been divided into three groups based on the route of delivery and the frequency of delivery of their antibiotics. During surgery, samples of venous blood, joint fluid, and approximately one square centimeter of muscle will be taken from the patient and submitted to the clinical investigation division of Lilly for Keflin assay. Their clinical response of the patient will also be followed.

Personnel: None.

Funding: None.

PROGRESS

This project was initiated to deliver intravenous Keflin preoperatively to patients undergoing total joint surgery and to harvest bone samples at the time of joint replacement. These were to be sent to the drug company for antibiotic determinations in bone. To date, only two samples have been sent and no reply has been received. Since the inception of this study numerous articles have appeared in the orthopaedic literature rendering this project with such a small sampling obsolete.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Contrast and Spatial Frequency Sensitivity as a Screening Test
for Retinal Disease.

WORK UNIT NO.: C-11-78

PRINCIPAL INVESTIGATOR: Antonio San Martin, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: John P. Shock, M.D., COL, MC

OBJECTIVES

To determine the usefulness of a new test, in which patients are asked to view printed sinusoidal gratings of varying contrast, as an indicator of retinal disease.

TECHNICAL APPROACH

Arden's test will be administered to patients with documented retinal pathology and to a comparable set of age-matched controls. The test involves looking at a series of five sheets of paper and indicating if and when a pattern is seen on the paper. Results will be categorized when a sufficient number of patients have been seen to give statistical significance.

Personnel: None.

Funding: None.

PROGRESS

This study was terminated due to transfer of principal investigator.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Oxytrode Sensor and the Clinical Utility of Concurrent Continuous Measurement of Arterial and Central Venous PO_2 .

WORK UNIT NO.: C-18-78

PRINCIPAL INVESTIGATOR: Richard C. Traugott, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Robert L. Treasure, M.D., COL, MC; Robert L. Watson, M.D., COL, MC; Raymond J. Will, M.D., MAJ, MC; Mr. Aubrey O. Bailey

OBJECTIVES

To evaluate accuracy, safety, feasibility, and clinical utility of the OXYTRODE Sensor for continuous measurement of arterial and mixed venous PO_2 during cardiopulmonary bypass by measurement and/or observation of:

a. Accuracy - by statistically valid comparison with conventional intermittent sampling.

b. Safety - by observation of the lack of occurrence of any adverse effects unforeseen in preclinical testing.

c. Feasibility - by Observation of such practical considerations as requirements for operational space, setup time, calibration, records storage, packaging, etc.

d. Clinical utility - by obtaining investigators evaluation of the OXYTRODE Sensor relative to current methodology.

To evaluate clinical utility of concurrent continuous measurement of arterial and mixed venous PO_2 difference.

TECHNICAL APPROACH

Patients undergoing non-emergency surgery using cardiopulmonary bypass via a pump-oxygenator in which bypass time is expected to equal or exceed one hour will be entered into the study. A written record will be kept of oxygen concentration being added to oxygenator, the flow rate of the pump, and clock times of all changes in these values.

C-18-78 (Continued)

Continuous simultaneous strip chart recording will be made of PO_2 as measured by one OXYTRODE Sensor placed in the arterial and another in the venous line of the pump. Intermittent arterial and central venous PO_2 samples will be drawn and measured in the conventional manner.

Personnel: None.

Funding: None.

PROGRESS

Final analysis of the data has not been completed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Study of Intraocular Lenses

WORK UNIT NO.: C-21-78

PRINCIPAL INVESTIGATOR: John P. Shock, M.D., COL, MC

ASSOCIATE INVESTIGATORS: John V. Van Gemert, M.D., MAJ, MC; George G. Lowell, M.D., LTC, MC; Harry W. Flynn, M.D. MAJ, MC

OBJECTIVES

To establish the safety and effectiveness of this device for use in human subjects according to guidelines recommended by the Food and Drug Administration ophthalmic advisory panel.

TECHNICAL APPROACH

Continuous monitoring of patients undergoing cataract extraction with insertion of intraocular lenses has been undertaken to satisfy the requirements of Part 812, Title 21 of the Code of Federal Regulations (Investigational Device Exemptions). Specific controls to facilitate the evaluation of the safety and efficacy of the intraocular lens are an integral part of this clinical study design.

Personnel: None.

Funding: None.

PROGRESS

The intraocular lens study began in February 1978. We have inserted 46 intraocular lenses following cataract surgery. Twenty-three of these lenses have been inserted in 1979. The two main lenses inserted are the Coburn (Choyce) anterior chamber lens and the McGhan (Worst Medallion) iris fixated lens. Two lenses had to be removed; one for persistent high pressures in the eye associated with hyphema and the other for persistent inflammation. One of these patients died from unrelated causes shortly after, and the other is doing well with standard contact lens correction. The remaining 44 patients are doing well with the intraocular lenses.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Intravesical Instillation of THIOTEPA at the Time of Transurethral Resection of Bladder Tumor.

WORK UNIT NO.: C-34-78

PRINCIPAL INVESTIGATOR: Stephen F. Richardson, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Mauro P. Gangai, M.D., COL, MC; Ritchie Spence, M.D., LTC, MC; Howard D. Solomon, M.D., MAJ, MC

OBJECTIVES

To study the use of THIOTEPA intravesical instillations at the time of transurethral resection of bladder tumors with regard to:

- a. Amount of THIOTEPA left in the bladder following the period of instillation and washout.
- b. Determination of serial blood levels of THIOTEPA following intravesical instillation at time of transurethral resection of bladder tumors.
- c. Prospective study to evaluate efficacy of intraluminal THIOTEPA at the time of transurethral resection of bladder tumors in prevention or delay of recurrent/residual bladder tumors.
- d. Monitoring patients carefully for evidence of toxicity, especially myelosuppression.

TECHNICAL APPROACH

At the time of surgery, THIOTEPA will be placed into the bladder immediately following removal of the tumor tissue. The drug will be allowed to remain in the bladder for 2 hours and then be washed out through a rubber catheter. Bladder washings will be sent to the laboratory to determine the amount of THIOTEPA remaining in the bladder after the 2 hour period. Blood samples will be taken at 1, 3, 5, and 8 hour intervals to determine the exact blood levels following absorption of THIOTEPA from the bladder.

Personnel: 1 SP5 (4 months)

Funding: None.

C-34-78 (Continued)

PROGRESS

Much time and effort were put into the development of the THIOTEPA assay without success. Without the assay, the study would be meaningless; therefore the protocol was terminated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Percutaneous Epidural Stimulation for Pain Relief During First Stage of Labor.

WORK UNIT NO.: C-40-78

PRINCIPAL INVESTIGATOR: John A. Scavone, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Robert M. Young, M.D., CPT, MC; Robert L. Watson, M.D., COL, MC; Alexander G. Juden, Jr., M.D., COL, MC; Richard R. Ritter, M.D., COL, MC

OBJECTIVES

To determine if epidural electrical stimulation is a safe and effective method of effecting analgesia in the first stage of labor. The theoretical basis for this experiment is to diminish "c" fiber mediated sympathetic pain during the first stage of labor by means of an epidural stimulator.

TECHNICAL APPROACH

Study patients are those who normally, because of their labor and attendant anesthetic requirements, elect to receive continuous lumbar epidural analgesia. Lumbar epidural catheter will be placed in the routine manner in the labor suite. The epidural catheter will consist of a standard teflon epidural catheter through which a flexible stainless steel wire has been inserted. Low frequency, weak, epidural stimulation will be delivered through the catheter using a standard Shimoji type pulse generator. Vital signs of the mother will be monitored and recorded at frequent intervals. Fetal heart rate and uterine contractions will be monitored and recorded simultaneously and continuously. Analgesia, if adequate, will be maintained via epidural stimulation during the first stage of labor and at the development of stage two of labor the patient receives a standard lumbar epidural anesthetic via the same catheter for delivery.

Personnel: None.

Funding: None.

PROGRESS

This project experienced a long technical delay in fabricating and testing the Shimoji type pulse generator to enable delivery of "saw

C-40-78 (Continued)

tooth" wave configuration of low frequency, weak voltage and delivery of no net current. Accordingly, only a small group of four patients were studied prior to the departure of the primary investigator. Under an approved protocol with our affiliated obstetrical anesthesia teaching program at the Robert B. Green Hospital, 15 additional patients were studied using this technique for pain relief in the first stage of labor. Six of these patients reported pain relief of 30% or more, only one patient reported more than 90% pain relief. All patients obtained uniform pain relief after injection of local anesthetic via the same catheter. Thus, catheter placement would seem to have been appropriate.

This trial of low frequency, low voltage epidural stimulation was considered unsuccessful in the management of the first stage of labor pain.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Dantrolene Sodium IV for Reduction of Lethal Effects of
Malignant Hyperthermia Crisis.

WORK UNIT NO.: C-3-79

PRINCIPAL INVESTIGATOR: Richard R. Ritter, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To ascertain the potential of dantrolene sodium IV for reduction of the lethal effects of the malignant hyperthermia crisis in affected patients.

TECHNICAL APPROACH

In addition to a rigid treatment program to follow in the event of development of a malignant hyperthermia reaction, dantrolene sodium is injected intravenously in doses of 1 mg/kilogram until tachycardia or arrhythmia is relieved or muscle tone or temperature decreases. Further infusions at the same dose level may subsequently be indicated if the heart rate increases or again becomes irregular or if the muscle tone or temperature again increases.

Personnel: None

Funding: None.

PROGRESS

No indication has developed for the use of this protocol. However, this investigation project will be kept active until the investigational drug has been released for general usage by the Food and Drug Administration.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Analgesic Effect of Epidurally Administered Morphine.

WORK UNIT NO.: C-15-79

PRINCIPAL INVESTIGATORS: Richard R. Ritter, M.D., COL, MC; L. Jack Hempling, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Staff and Residents, Anesthesia and Operative Service

OBJECTIVES

To evaluate the analgesic effect of extradural administration of morphine and its potential side effects to include vascular reabsorptive levels.

TECHNICAL APPROACH

Participants in this study are those patients who would normally, because of the nature of the surgery and anesthetic requirements, elect to receive continuous epidural anesthesia. Following completion of the surgical procedure and at the time of return of sensory function (i.e. pain), an injection of either 5 or 10 mgs morphine in 10 cc normal saline is administered through the epidural catheter. The patient is then observed for any complications or adverse side effects. Blood samples are taken from a previously placed intravenous catheter at 15 minutes, 1, 2 and 4 hours. Blood levels of morphine are measured or determined by electron capture gas liquid chromatography. The duration of analgesia afforded from epidural morphine injection is recorded. Patients receive standard postoperative analgesia prescribed by the primary physician if there is not at least 50% subjective analgesia relief from the epidural injection within 15 minutes.

Personnel: None.

Funding:

FY 79

Contractual Service

\$3,000.00

C-15-79 (Continued)

PROGRESS

Fifteen patients have been entered thus far into the study and blood samples submitted to the Pathology Department of the University of Texas Health Science Center for analysis. Reassignment of the principal investigator has delayed completion of this study; however, it will be continued by an associate investigator.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Antiplatelet Therapy in Carotid Endarterectomy.

WORK UNIT NO.: C-32-79

PRINCIPAL INVESTIGATOR: V. T. Deal, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Bruce S. Jarstfer, M.D., COL, MC

OBJECTIVES

To determine intraoperative blood loss and quantitate postoperative blood loss by estimate of wound hematoma volume in patients receiving or not receiving antiplatelet therapy in the perioperative period.

TECHNICAL APPROACH

Double blinded administration of ASA vs. placebo to patients will begin 6 days prior to carotid endarterectomy. Careful measurement of intraoperative blood loss will be carried out, and postoperative wound complications will be evaluated.

Personnel: None.

Funding: None.

PROGRESS

This is a new project.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy of Epirizole in the Treatment of Swelling Accompanying Dental Surgery.

WORK UNIT NO.: C-4-79

PRINCIPAL INVESTIGATOR: Sterling R. Schow, D.M.D., LTC, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if epirizole therapy, as compared to placebo, will prevent or significantly decrease the swelling which accompanies third molar extractions.
2. To evaluate the safety of epirizole therapy by close observation of the patients concerning organs, organ systems, clinical laboratory values and side effects and adverse reactions.

TECHNICAL APPROACH

The study has been conducted within the parameters outlined in the clinical protocol with appropriate amendments as approved by the Human Subjects Research Review Board on 16 October 1978. The study was initiated 27 April 1979 with treatment of the first patient. To date a total of six patients have completed study strictly within the outlines of the protocol. Data are collected daily and relayed via telephone-computer transmission to the sponsor, Marion Laboratories, in Kansas City for analysis.

Personnel: None.

Funding: None.

PROGRESS

Even though this investigation is a double-blind study, no significant clinical difference has been noted in any of the patients who have completed treatment when comparing third molar removal on the right side versus identical treatment on the left.

Analysis of data received by researchers at Marion Laboratories from this and similar studies at other locations is being continued. A

C-4-79 (Continued)

meeting with these investigators in mid-October 1979 is planned to make a decision to either continue or discontinue the study.

There have been no side effects or adverse reactions in any of the study patients nor have there been alterations in physical status or laboratory values which can be associated with the study medication.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Reduction of Low Back Pain as a Function of the Interaction of Physical Therapist and Patient. (Health Care Study)

WORK UNIT NO.: C-43-77

PRINCIPAL INVESTIGATOR: Jane E. Gierhart, LTC, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To investigate the treatment of low back pain and evaluate both the physical treatment of the patient and the interaction between physical therapist and patient.

TECHNICAL APPROACH

Utilizing questionnaires furnished the MEDDAC/MEDCEN by the principal investigator, information about the patient's low back pain and the treatment will be collected. For purposes of this study, low back pain is defined as any pain of acute or chronic nature from T-10 to the tuberosity of the ischium.

Personnel: None

Funding: None

PROGRESS

Data are being statistically evaluated.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Pool Therapy for Medial Meniscectomy Patients.

WORK UNIT NO.: C-27-78

PRINCIPAL INVESTIGATORS: Jane M. Huffaker, 2LT, AMSC
Carol E. Petersen, 2LT AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the effects of a specific therapeutic swimming program on knee range of motion and quadriceps strength following medial meniscectomy.

TECHNICAL APPROACH

Ten patients participated in the study. There were nine males and one female ranging in age from 18-28 years, and all had undergone medial meniscectomy. All patients received identical preoperative and post-operative treatment until the time of suture removal at approximately two weeks post-surgery. The patients were then divided equally between two groups, a clinic (control) group and a pool (experimental) group. The clinic group followed a standard strengthening program twice a day, while the pool group substituted the afternoon clinic session with pool therapy.

Personnel: None.

Funding: None.

PROGRESS

Quadriceps strength improvement over the three-week treatment period was not statistically different between the two groups. However, subjective findings support the success of the pool program in terms of the psychological benefits inherent in swimming.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Equivalent Temperature Changes Caused by Infrared and Ultrasound on the Sensory Conduction Latency of the Superficial Radial Nerve in Man.

WORK UNIT NO.: C-28-78

PRINCIPAL INVESTIGATORS: John S. Halle, 2LT, AMSC;
Charles R. Scoville, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if the sensory nerve conduction latency of the superficial radial nerve in man is affected equally by equivalent temperature increases induced by infrared energy and ultrasonic energy.

TECHNICAL APPROACH

Ten healthy adult subjects, six males and four females, received ultrasound and infrared treatments to create a 1.2°C increase in subcutaneous tissue temperature. Nerve conduction latencies were recorded for each 0.3°C increase during both the ultrasound and infrared treatments. The latencies were analyzed using a two way analysis of variance and a matched group student's "t" statistical technique.

Personnel: None.

Funding: None.

PROGRESS

The combined mechanical and heating effects of ultrasound caused a similar decrease in latency of the lateral cutaneous branch of the radial nerve as did the heating effects of infrared. The obtained data indicated that ultrasound's mechanical effects did not play a significant role in effecting the nerve conduction latency.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Patient Applied vs. Therapist Applied Ultrasound for the Treatment of Plantar Warts: A Comparative Study.

WORK UNIT NO.: C-29-78

PRINCIPAL INVESTIGATORS: Raymond C. Ronat, 2LT, AMSC;
Richard G. Simmons, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if there is any difference in cure rates between patient applied and therapist applied ultrasound for the treatment of plantar warts.

TECHNICAL APPROACH

Forty patients diagnosed as having Verruca plantaris (plantar warts) were divided into two groups in which one group received ultrasound administered by a member of the physical therapy staff while the other group applied the treatment to themselves.

Personnel: None.

Funding: None.

PROGRESS

The patient-applied group had a slightly better cure rate than did the therapist-applied group (80% versus 70%, respectively). These results were consistent with those of previous researchers and well above the level of 55% which has been estimated as the spontaneous cure rate. Therefore, self-administration of ultrasound for the treatment of plantar warts appears to be an effective treatment modality.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Perceived Vs. Subliminal Stimulus TENS on Pain Threshold.

WORK UNIT NO.: C-30-78

PRINCIPAL INVESTIGATOR: Frank B. Underwood, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if there is any difference in the pain threshold of normal subjects before and during the application of an electrical stimulus.
2. To determine if there is any difference in the pain threshold of normal subjects during the application of subliminal versus perceived stimulus transcutaneous electrical nerve stimulation (TENS).

TECHNICAL APPROACH

The effects of two types of TENS on pressure pain threshold was studied. Sixteen normal subjects served as their own controls. The pain threshold was determined on the ulnar border of the hand using a household scale with a bolt attached to the platform. A five minute treatment with either a perceived stimulus or a subliminal stimulus TENS unit was then administered. The electrodes were placed over the ulnar nerve at the elbow and on the middle phalanx of the fifth digit. The post-treatment threshold was then determined, and the entire procedure repeated using the other stimulator.

Personnel: None.

Funding: None.

PROGRESS

A two-way analysis of variance (ANOVA) indicated significant main effects for treatment, but not for type of stimulator. A Scheffé's test indicated a significant mean comparison between the pre-treatment and post-treatment subliminal stimulator pain threshold means. It was concluded that subliminal stimulus is significantly more effective in increasing pressure pain threshold than perceived stimulus TENS.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Media Testing of Patient Education Video Tape 1092: "Open Heart Surgery and Physical Therapy".

WORK UNIT NO.: C-31-78

PRINCIPAL INVESTIGATORS: Stephen D. Ryan, 2LT, AMSC
Gaetano G. Scotece, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To date none of the video tapes for physical therapy patient education at BAMC have been formally evaluated. This project represents a pilot study of the effectiveness and validity of these teaching aides with regard to their prospective audiences.

TECHNICAL APPROACH

Twenty-eight patients participated in a study evaluating the quality of a patient education program based on a system of videotapes. All participants were candidates for a coronary artery bypass graft. The particular videotape selected for study pertained to the role of physical therapy in treating open heart surgery patients. Patients were divided into two groups on a random basis. Patients in Group I were pre-tested, prior to reviewing the videotape, and then post-tested. Patients in Group II were not pre-tested, but did take the post-test after viewing. A t-test was used to compare results.

Personnel: None.

Funding: None.

PROGRESS

The previewing test apparently had no effect on the post-test scores, and the patients did learn useful and practical information from viewing the videotape. This was evidenced by the correlation of scores on the post-test taken by both groups.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparative Study of Energy Consumption Between Normal Treadmill Walking Vs. Walking While Grasping Horizontal Handrails.

WORK UNIT NO.: C-32-78

PRINCIPAL INVESTIGATORS: Kerry Z. Huston, 2LT, AMSC;
Kathleen R. Westfall, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To measure the difference in oxygen consumption in normal walking at three miles per hour (4.83 km per hour) on a 9% grade while grasping horizontal handrails vs. walking with the arms freely swinging.

TECHNICAL APPROACH

Subjects were tested after three practice sessions of 10 min. duration each on the treadmill set at 3.5 mph, 9% grade. Equal practice of holding and not holding horizontal handrails was performed.

Testing included two tests randomly scheduled in holding-not holding sequence. each of 15 minutes duration. Respired gas was collected the last 1½-2 min. of the 15 min. walk, and analyzed for oxygen consumption values.

Personnel: None.

Funding: None.

PROGRESS

Ten subjects were tested. There was a significant decrease in $\dot{V}O_2$ while using hand support (20.38 ± 3.3 ml/kg/min versus 24.36 ± 2.6 ml/kg/min, mean \pm SD, $P < 0.01$). This decrease in $\dot{V}O_2$ was considered less than that which would be seen in any patient population.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Degree of Knee Extension as it Relates to
Symptomatic Chondromalacia Following Physical Exercise.

WORK UNIT NO.: C-36-78

PRINCIPAL INVESTIGATORS: Pamela E. Prentice, 2LT, AMSC
Deborah J. Robertson, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the relationship between the degree of knee extension and symptomatic chondromalacia following a prolonged exercise program.

TECHNICAL APPROACH

Forty-one female army officers were measured for knee extension using a universal double arm goniometer while standing on one leg. Of these, 23 demonstrated knee hyperextension, and 18 did not. These subjects were then tested for chondromalacia patellae using a modified compression test. Subjects who initially exhibited chondromalacia patellae were eliminated from the study. The remaining individuals were put through three weeks of an officer's physical training program. Following this program, the individuals who participated were again tested for chondromalacia patellae.

Personnel: None.

Funding: None.

PROGRESS

Of the subjects who were hyperextended, five showed symptoms of chondromalacia patellae and 18 did not. Of the 18 who were not hyperextended, two reported positive compression tests.

In this study it was determined that there was no difference between hyperextended and nonhyperextended women in the occurrence of symptomatic chondromalacia patellae following a prolonged exercise program.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Effects of the Application of Transcutaneous Electrical Nerve Stimulation on Peripheral Cutaneous Temperature as Measured in the Great Toe.

WORK UNIT NO.: C-37-78

PRINCIPAL INVESTIGATOR: Elizabeth J. Finan, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether TENS can alter peripheral blood flow.

TECHNICAL APPROACH

Nine healthy subjects received TENS to the tibial, superficial peroneal and deep peroneal nerves to determine TENS effects on surface temperature of the great toe. Change in blood flow was inferred from change in skin temperature.

After a steady state temperature was established, subjects received 20 minutes of TENS from a two channel Stimtec unit. Temperature recordings were taken at five minute intervals from both the stimulated and non-stimulated great toes. The tibial nerve was stimulated behind the medial malleolus, and the two peroneal nerves were stimulated as they entered the dorsum of the foot, just lateral to the extensor hallucis longus tendon.

Personnel: None.

Fundint: None.

PROGRESS

TENS had no direct or indirect effects on surface temperature of the stimulated or nonstimulated toes, and so apparently had no effect on cutaneous blood flow.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Heart Rate Response in Normal Subjects to Use of the Blow Bottle and the Spirocare Unit: Comparison with the Response to the Valsalva Maneuver.

WORK UNIT NO.: C-38-78

PRINCIPAL INVESTIGATOR: John Fromuth, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine and compare the heart rate response in normal subjects while using a blow bottle, while using a spirocare unit, and while performing a Valsalva maneuver.

TECHNICAL APPROACH

The study was carried out by having 18 subjects perform each of the three respiratory maneuvers for a period of 15 seconds each, during which heart rate was monitored using lead two of an EKG. The EKG strips were then analyzed to calculate the Valsalva ratio for each performance. These values were used to calculate the mean ratio for group performance of the three respiratory maneuvers.

Personnel: None.

Funding: None.

PROGRESS

A one way analysis of variance between groups was performed which showed significant difference between the effect of the spirocare and that of the blow bottle and Valsalva but no significant difference between the effects of the blow bottle and Valsalva. In view of these initial findings, perhaps a greater concern is needed on the part of therapists to evaluate a patient's cardiac status more closely before use of the blow bottle is initiated.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Relationship Between Grip Size of a Tennis Racquet and the Incidence of Tennis Elbow Symptoms in Female Tennis Players.

WORK UNIT NO.: C-19-79

PRINCIPAL INVESTIGATOR: Kathleen S. Zurawel, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the relationship between tennis elbow symptoms in female tennis players and variances in racquet grip size from true grip size of the individual as determined by measuring from the proximal palmar crease of the hand along the radial border of the ring finger to its tip.

TECHNICAL APPROACH

A random sample of female tennis players from local tennis clubs will be surveyed on site by a questionnaire and interview for grip size used, frequency of play, weight of racquet, and other factors which might contribute to symptomatic tennis elbow. Any player who has had pain in the elbow which has caused them to curtail their activities and stop playing tennis for a week or more, will be classified as having had symptomatic tennis elbow.

Personnel: None

Funding: None.

PROGRESS

Data collection has been completed, and analysis is in progress.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Quality Assurance in Physical Therapy: An Attitudinal Survey
on Specialization and Mandatory Continuing Education.

WORK UNIT NO.: C-20-79

PRINCIPAL INVESTIGATOR: Michael B. Hammond, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the attitudes of selected American Physical Therapy Association (APTA) members on the issues of specialization and mandatory continuing education.
2. To assess significant differences in the attitudes of selected APTA members on specialization and mandatory continuing education according to demographical data.

TECHNICAL APPROACH

A 48-item questionnaire was prepared to assess the attitudes of physical therapists on the issues of specialization and mandatory continuing education. From the population of Texas American Physical Therapy Association members, two hundred therapists were randomly selected to receive the questionnaire.

Personnel: None.

Funding: None.

PROGRESS

Completed questionnaires have been received and await computerized processing to determine the outcome. A statistical analysis will be performed on the results of this survey utilizing the Statistical Package for the Social Sciences.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

Investigation Project Resume

TITLE: Input by Clinical Faculties into the Curriculum Content and Design of Entry-Level Therapy Programs.

WORK UNIT NO.: C-24-79

PRINCIPAL INVESTIGATOR: Neva C. Gaskins, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the extent of input clinical faculties have in the Physical Therapy academic curriculum content and design.

TECHNICAL APPROACH

A questionnaire will be sent to a random sampling of the population of clinical facilities in the CONUS which sponsor physical therapy student affiliation. The questionnaire is designed to gather information concerning the input that clinical supervisors have into physical therapy programs in terms of curriculum and student selection and evaluation.

Personnel: None.

Funding: None.

PROGRESS

The questionnaires have been mailed, but no responses have been received.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Survey of Participation of U.S. Army Physical Therapists in Continuing Education.

WORK UNIT NO.: C-25-79

PRINCIPAL INVESTIGATORS: Richard Bozzio, 2LT, AMSC;
Debra Chang, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the percentage of U.S. Army physical therapists who participated in continuing education during calendar year 1978.
2. To develop a profile of the "typical Army physical therapist" based on the factors influencing their participation.

TECHNICAL APPROACH

One hundred and fifty-eight questionnaires have been mailed to to U.S. Army physical therapists in CONUS, Alaska, and Hawaii. These will be analyzed to determine (1) the average amount of personal funds spent for continuing education (CE) during calendar year 1978; (2) the average amount of TDY funds spent for CE during calendar year 1978; (3) the most prevalent rea of special interest; (4) the most preferred method of CE; and (5) the number of physical therapists who are licensed in a state that requires mandatory CE.

Personnel: None.

Funding: None.

PROGRESS

Responses to questionnaires are being evaluated.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Biofeedback Treatment of Extensor Lag After Total Knee
Arthroplasty Compared with Standard Rehabilitation Technique:
Effects on Time of Recovery.

WORK UNIT NO.: C-27-79

PRINCIPAL INVESTIGATORS: Gary Hague, 2LT, AMSC;
Richard Petersen, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if electromyographic (EMG) biofeedback when used as an adjunct to a standard rehabilitation program for total knee arthroplasty patients is effective in reducing the amount of time needed to correct extensor lag.

TECHNICAL APPROACH

All patients presenting for total knee surgery at Brooke Army Medical Center and Wilford Hall USAF Hospital with an extensor lag of 15° or more postoperatively are being considered for the study. Those chosen for the experimental group are administered EMG audiovisual biofeedback during quadriceps exercise as an adjunct. Those in the control group receive quadriceps exercise without EMG biofeedback. Data concerning active extension and passive extension are being collected preoperatively, directly postoperatively, and every seven days postoperatively until a three week postoperative period has been reached.

Personnel: None.

Funding: None.

PROGRESS

Data are being collected.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Transcutaneous Electrical Nerve Stimulation on
Quadricep and Hamstring Muscle Power in Patients with
Symptomatic Chondromalacia Patellae.

WORK UNIT NO.: C-28-79

PRINCIPAL INVESTIGATOR: Robin E. Yates, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate any change in quadricep and hamstring muscle power in patients with painful chondromalacia after an application of transcutaneous electrical nerve stimulation (TENS) to recommended knee pain points.

TECHNICAL APPROACH

The experimental group will be tested on the Cybex isokinetic dynamometer during the initial session and the maximum torque recorded. During the second session, this group will be retested on the Cybex, followed by a TENS treatment to acupuncture points recommended for knee pain, and then retested on the Cybex. On the third day, a final Cybex test will be performed. Like the experimental group, the control group will be tested on the Cybex four times over a period of three sessions. This group, however, will not receive TENS treatment during the second session; instead, the subject will rest for twenty minutes.

Personnel: None.

Funding: None.

PROGRESS

This is a new study, and no reportable results have been obtained.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Relationship Between the Pain of Chondromalacia Patellae and Knee Range of Motion.

WORK UNIT NO.: C-29-79

PRINCIPAL INVESTIGATOR: Mary Petlin, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine what portion of the normal range of knee motion, between 90 degrees of flexion and zero degrees of extension, is painful for patients with chondromalacia patellae when exercising against maximum resistance.

TECHNICAL APPROACH

Patients with chondromalacia patellae and no other knee pathology will be tested on the Cybex II isokinetic dynamometer using the slow velocity torque-curve test. Both knees will be tested beginning at 90° flexion through full extension. The strength and shape of the torque curves plotted for each knee will be compared to rule out malingering or sub-maximal effort. The portion of the curve in which artifacts appear, indicating a lesser effort due to pain, will be marked off. The arc of motion that this portion represents will be calculated. Results will be compared and a mean-range calculated.

Personnel: None.

Funding: None.

PROGRESS

Six patients have been tested for a total of nine knees. These results have not yet been compiled.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Study of Mastectomy Patients: Psychological Adjustment Problems and What Can Be Done to Help.

WORK UNIT NO.: C-30-79

PRINCIPAL INVESTIGATORS: Diana Felten, 2LT, AMSC;
Joan Beebe, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To investigate the psychological problems and concerns encountered by the mastectomy patient as she seeks to adjust to the loss of a breast and the diagnosis of cancer.
2. To determine beneficial sources of help to include internal psychological coping mechanisms such as positive thinking, and external sources such as group or family support.

TECHNICAL APPROACH

Questionnaires will be sent to a minimum of 50 mastectomy patients who are between 1 and 5 years postoperative. Data will be analyzed by means of descriptive statistics and will consist of information regarding psychological problems encountered and adjustments made through either internal or external sources of help.

Personnel: None.

Funding: None.

PROGRESS

Questionnaires have been mailed; however all responses have not been received.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: TENS Applied at an Acupuncture Point to Facilitate Recovery of Postoperative Knee Patients.

WORK UNIT NO.: C-31-79

PRINCIPAL INVESTIGATORS: Barry L. Karalfa, 2LT, AMSC;
J. Wesley McWhorter, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effectiveness of TENS applied via an acupuncture point in reducing pain thereby allowing a faster recovery of postoperative knee patients.

TECHNICAL APPROACH

As postoperative knee patients are referred to the clinic, they are immediately begun on the post surgical knee rehabilitation program. After an explanation of the project and with the patient's consent, they are randomly assigned to an experimental or control group. Both groups are connected to a TENS unit with the experiment group receiving a 20 minute treatment and the control group receiving a simulated treatment with the unit turned off. A subjective assessment of the patient's pain level is obtained prior to and immediately following the TENS treatment and following the exercise protocol. When possible range of motion measurements are taken at these times.

Personnel: None.

Funding: None.

PROGRESS

To date five patients have been included in the project, three in the control group and two in the experimental group. Patient acquisition will be continued.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Heart Rate Response to the Valsalva Maneuver when Performed
During Exercise.

WORK UNIT NO.: C-33-79

PRINCIPAL INVESTIGATOR: Mary Reidelbach, 2LT, AMSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effects of the Valsalva maneuver on heart rate when performed during the partial sit-up exercise in normal subjects.

TECHNICAL APPROACH

A baseline EKG will be taken before exercise and subjects will perform the sit-up alone, the Valsalva maneuver alone, and finally the Valsalva maneuver with the sit-up exercise. The Valsalva maneuver will be simulated by blowing through a mouthpiece into a sphygmomanometer inflated to 30 mm and will maintain a pressure of 40 mm for five seconds. The EKG will be taken during exercise and will be used to determine changes in heart rate. A statistical analysis will be done and results determined.

Personnel: None.

Funding: None.

PROGRESS

Data collection still in progress.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Patient Attitudes and Feelings Related to Health and Life.

WORK UNIT NO.: C-16-79

PRINCIPAL INVESTIGATOR: Nancy Rassiga, Graduate Student, The Worden
School of Social Service

ASSOCIATE INVESTIGATOR: Stonell B. Greene, MAJ, MSC

OBJECTIVES

To determine if there is a relationship between patients' thinking about the condition of their health and their thinking about themselves as "growing older" in patients age 55 and older.

TECHNICAL APPROACH

The sample consisted of 40 persons age 55 and older who were in-patients at Brooke Army Medical Center. Subjects were randomly selected from four separate ward populations: female/male orthopaedics; female/male surgery wards.

To determine age perception, each person was asked to respond to the question "We would like to know how old you feel. Would you say you feel young, middle aged, old or very old?" Scored 1-4; young to very old.

Data concerning the second dependent variable, happiness, was measured by the question: "Taking all things together, how would you say things are these days? Would you say you are happy, pretty happy, or not too happy?" Scoring of this scale was in the direction of the higher scores being less favorable.

Personnel: None.

Funding: None.

C-16-79 (Continued)

PROGRESS

To the questions regarding age, the greatest number of respondents (47.5) classified themselves as middle aged; 25% said they were young. Only 20% identified with being old and 7.5% labeled themselves as being very old. The most significant predictor of perception of age was self-rated health, followed by age. The remaining variables of sex, education and income had smaller relationships with perception of age. These findings indicate that people who are healthier tend to view themselves as younger.

In the analysis of self-rated happiness, the most important predictor was health, followed by age.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

APPENDIX A

Polycythemia Vera Study Group

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Thrombosis in Patients with Polycythemia Vera.

WORK UNIT NO.: PVSG-5

PRINCIPAL INVESTIGATOR: Charles T. Thornsvar, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

To determine whether phlebotomy in conjunction with antiaggregating agents can decrease the frequency of thrombotic complications in patients with PV to the level in patients treated with ³²P.

TECHNICAL APPROACH

Eligibility: Only those patients who have well-documented, active polycythemia vera, as demonstrated by rigorous diagnostic studies designed to eliminate spurious (stress) polycythemia, anoxic erythrocytosis, or erythrocytosis secondary to increased erythropoietin, or erythrocytosis without additional evidence of myeloproliferative disease either past or present, will be eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

82 patients have been randomized to this study. Follow-up time is, as yet, insufficient to present meaningful data.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Acute Leukemia Preceded by Polycythemia Vera.

WORK UNIT NO.: PVSG-6

PRINCIPAL INVESTIGATOR: Charles T. Thornsvar, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

1. To determine the characteristics of the leukemic transformation in polycythemia vera.
2. To determine what fraction of patients with this disorder will respond to vincristine and prednisone chemotherapy.
3. To determine if chemotherapy, designed for patients with acute myeloblastic leukemia, is useful in the treatment of leukemic transformation.

TECHNICAL APPROACH

Eligibility: Only those patients who have well-documented polycythemia vera as demonstrated by rigorous diagnostic studies, as described in the protocol, will be eligible for this study.

Therapy will follow the schema outlined in the protocol.

PROGRESS

Thirteen patients have been studied of whom 61% are males. The average age at onset of polycythemia was 60 years, and the average age of death was 66 years. The average time between the diagnosis of P.V. and acute leukemia was 6 years. The shortest interval to the development of leukemia was one year, the longest 11 years. It appeared as if there was no difference in the interval between those treated with radioactive phosphorus compared to those treated with alkylating agents

PVSG-6 (Continued)

alone. Some of the patients had been treated with multiple myelo-suppressive agents. Of 10 patients who received a full course of therapy, there were no responses. Of the 10 patients who failed Vincristine and Prednisone, 5 were eventually treated with Adriamycin and Cytosine Arabinoside. Of this number, 3 died during the induction phase (within the first 30 days). Two achieved partial remissions. Of these, one patient went on to maintenance therapy, a second had a second course of chemotherapy and that patient subsequently died. The median survival for the entire group from the point of diagnosis of acute leukemia was 30 days. Many of the patients died secondary to sepsis.

The conclusions were that there was no evidence that Vincristine and Prednisone therapy exerted antileukemic effect in post-polycythemic patients. This study will remain open until a new protocol can be prepared.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Efficacy Trial using POTABA in Treatment of Post-Polycythemia and Agnogenic Myeloid Metaplasia.

WORK UNIT NO.: PVSG-7

PRINCIPAL INVESTIGATOR: Charles T. Thornsvar, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

To determine by bone marrow section examination, whether Potaba has any antifibrosing action in patients with PPMM and AMM.

TECHNICAL APPROACH

Eligibility: All asymptomatic patients with PPMM and AMM, as defined in the study protocol, are eligible. Patients with AMM or PMMM who have had previous chemotherapy or androgens or steroids will be eligible for the study providing (1) they have been off chemotherapy for a period of at least two months; (2) they have been off prednisone or androgens for a period of at least one month.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Thirty-four patients are entered into the study, but the accrual rate has decreased within the last year. Of the 34 patients entered on study, only 2 were symptomatic at the time of randomization. There was no significant drug toxicity in any of the patients entered. The results of this study are inconclusive.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy Trial Using Hydroxyurea (HU) in Polycythemia Vera.

WORK UNIT NO.: PVSG-8

PRINCIPAL INVESTIGATOR: Charles T. Thornsvar, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

To evaluate the efficacy of HU in patients of all ages with polycythemia vera who have active disease and to assess the influence of HU upon the symptoms and signs of active disease and upon the abnormal hematological and biochemical manifestations of the panmyelosis that characterize this condition.

TECHNICAL APPROACH

Eligibility: Only those patients who have well-documented, active polycythemia vera, as demonstrated by rigorous diagnostic studies designed to eliminate spurious (stress) polycythemia, anoxic erythrocytosis, or erythrocytosis secondary to increased erythropoietin, or erythrocytosis without additional evidence of myeloproliferative disease either past or present, will be eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

The coexistence of iron deficiency as indicated by persistently low mean corpuscular volumes has led to difficulty in evaluating the response to HU in terms of both control in hematocrit and control of thrombocytosis. Accordingly, an addendum to the protocol specifies that patients must be replaced with iron if there is evidence of iron deficiency in order that the full effect of HU may be evaluated.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Randomized Trial Comparing Splenectomy vs. 32-P
vs. Alkeran for the Complications of Splenomegaly in Myelo-
proliferative Disorders.

WORK UNIT NO.: PVSG-9

PRINCIPAL INVESTIGATOR: Charles T. Thornsward, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

1. To determine the effects of a short course of high dose prednisone on the hemolytic process associated with splenomegaly in myeloproliferative disorders.
2. To determine, in those patients whose hemolytic anemia is refractory to prednisone therapy, in a prospective randomized trial, the value of splenectomy vs. alkylating agents.
3. To study the effects of high dose prednisone on thrombocytopenia in patients with myeloproliferative disorders.
4. To determine, in those patients whose thrombocytopenia is refractory to prednisone therapy, in a prospective randomized trial, the value of splenectomy vs. supportive care alone.
5. To study the effects of a short course of high dose prednisone on the pain and mechanical discomfort caused by an enlarged spleen.
6. To determine, in those patients whose pain and mechanical discomfort is refractory to prednisone therapy, in a prospective randomized trial, the results of splenectomy vs. those of alkylating agents.

TECHNICAL APPROACH

Eligibility: Patient eligibility is as outlined in the study protocol.

PROGRESS

Only six patients have been entered on the study. It is too early to report any meaningful results.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Thrombosis in Myeloproliferative Disease Other Than Polycythemia Vera.

WORK UNIT NO.: PVSG-10

PRINCIPAL INVESTIGATOR: Charles T. Thornsvarð, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

To prevent and control the symptoms of bleeding and thrombosis associated with (1) the clinical entity, primary thrombocytopenia, (2) those patients with myelofibrosis-myeloid metaplasia with elevated platelet counts, and (3) those patients with classified myeloproliferative disease with elevated platelet counts.

TECHNICAL APPROACH

Eligibility: Those patients with the entity - primary thrombocythemia, myelofibrosis, myelosclerosis and unclassifiable myeloproliferative disease shall be eligible for randomization between ^{32}P and Alkeran provided they meet the requirements outlined in the protocol.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

A total of 41 patients with primary thrombosis are evaluable. The data indicated that both Alkeran and ^{32}P were comparably effective in achieving good responses in patients with primary thrombocytosis within a period of three months. The overall response rate for Alkeran was approximately 90% and 70% for radioactive phosphorus. There was no significant toxicity with either agent.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Anemias with or without Cytopenia in Myeloproliferative Disease.

WORK UNIT NO.: PVSG-11

PRINCIPAL INVESTIGATOR: Charles T. Thornsvard, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

To evaluate the use of high dose androgens both orally and parenterally in a randomized clinical trial in patients with myeloproliferative disease whose primary problem is a resistant anemia, and in some instances, is associated with single or multiple cytopenia.

TECHNICAL APPROACH

Eligibility: All patients with a myeloproliferative disorder with anemia who are unresponsive to iron, B₁₂, folate and/or pyridoxine will be eligible for this study. All previously untreated patients will be eligible provided they are symptomatic and meet the criteria outlined in the study protocol.

All patients will be randomized between oral androgen and intramuscular androgen as outlined in the study protocol.

PROGRESS

There has been no significant toxicity as yet and there have been no problems with intramuscular injections in patients with thrombocytopenia. The preliminary data suggest that there may be differences in response to the two modalities of androgen therapy.

Status: Ongoing.

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Study of the Clinical Features and Natural History of Asymptomatic Patients with Myeloproliferative Disorders.

WORK UNIT NO.: PVSG-13

PRINCIPAL INVESTIGATOR: Charles T. Thornsvard, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

1. To obtain a clinical and laboratory data base on patients with myeloproliferative disorders prior to the time they require treatment under other MPD protocols.
2. To define the natural course of the disease as to the development of: a) splenomegaly; b) progressive fibrosis; c) leukemic conversion; d) thromboembolic complications and e) other neoplasm.
3. To demonstrate the development of cytogenetic and pathologic abnormalities in bone marrow and peripheral blood.
4. To establish predictors of a more symptomatic stage of the disease.

TECHNICAL APPROACH

Eligibility: All newly diagnosed (less than one year), previously untreated patients (including patients transfused for a period of less than three months) considered to have one of the myeloproliferative disorders outlined in the protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy Trial using Cimetidine for Pruritus in Polycythemia Vera.

WORK UNIT NO.: PVSG-14

PRINCIPAL INVESTIGATOR: Charles T. Thornsvar, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Glenn M. Mills, M.D., CPT, MC

OBJECTIVES

To determine whether H₂ antagonists are efficacious in alleviating the pruritus of polycythemia vera.

TECHNICAL APPROACH

Eligibility: Only those patients who have well-documented, active polycythemia vera, as demonstrated by diagnostic studies designed to eliminate spurious (stress) polycythemia, anoxic erythrocytosis, or erythrocytosis secondary to increased erythropoietin, or erythrocytosis without additional evidence of myeloproliferative disease either past or present, will be eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Three patients have been formally entered on this study. Information has been received on 9 other patients who were treated with Cimetidine. Of the 12 patients, 5 good responses were recorded and 2 partial responses.

Status: Ongoing.

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

APPENDIX B

Gynecology Oncology Group

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Melphalan Alone vs. Adriamycin and Cyclophosphamide vs Hexamethylmelamine and Melphalan in Patients with Ovarian Adenocarcinoma: Suboptimal Stage III, Stage IV, and Recurrent Equivalent to Stages III and IV (Phase III).

WORK UNIT NO.: GOG 22

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if combination chemotherapy is more effective than Melphalan alone in achieving remission and improving survival in Stage IV and suboptimal patients with Stage III ovarian cancer.

TECHNICAL APPROACH

Patient Eligibility: Patients who have been diagnosed as Stage IV and suboptimal Stage III primary cases together with recurrent cases equivalent to Stage III and IV.

Patients will be randomized to one of three treatment programs, and therapy will follow the schema outlined in the study protocol.

PROGRESS

There is no significant difference comparing the three regimens comparing response versus no response. Complete response rate is significantly lower for the Melphalan alone limb of the study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Women with Cervical Cancer Stage IIB, IIIB, IVA, Confined to the Pelvis and/or Para-aortic Nodes with Radiotherapy Alone vs Radiotherapy plus Immunotherapy (Phase II).

WORK UNIT NO.: GOG 24

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To assess the therapeutic effectiveness of immunotherapy (intravenous C-parvum) used concomitantly with radiation in patients with advanced carcinoma of the uterine cervix.

TECHNICAL APPROACH

Patient Eligibility: All patients with primary, previously untreated histologically confirmed invasive carcinoma of the uterine cervix, Stages II-B, III-B or IV-A (confined to the pelvis and para-aortic nodes).

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Of the 78 evaluable cases, 49 have measurable disease. To date, there have been 14 recurrences and 10 deaths. These small numbers preclude comparisons at this time. None of the deaths are considered treatment related.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Melphalan Therapy Alone vs Melphalan plus Immunotherapy (C. Parvum) in the Treatment of Women with Stage III (Optimal) Epithelial Carcinoma of the Ovary, Phase II.

WORK UNIT NO.: GOG 25

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of adjuvant nonspecific immunotherapy to standard alkylating agent therapy in patients with Stage III optimal carcinoma of the ovary.

TECHNICAL APPROACH

Patient Eligibility: Patients in "Optimal" category (3 cm or less greatest diameter of residual tumor(s) with proven primary Stage III epithelial cancer of the ovary) who have undergone tumor-reductive surgery will be included in this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Of those patients who received C-Parvum, 60.5% experienced chills/fever (primarily moderate), 5.3% hypersensitivity, 23.7% nausea and 33.3% nausea and vomiting.

Only 7 patients on the Melphalan alone limb had measurable disease; three have responded. Of 6 measurable-disease patients on the Melphalan plus Immunotherapy regimen, one has had a complete response and one has had partial response.

GOG 25 (Continued)

There is no significant difference when the duration of progression-free interval is compared by therapy.

Status: Ongoing.

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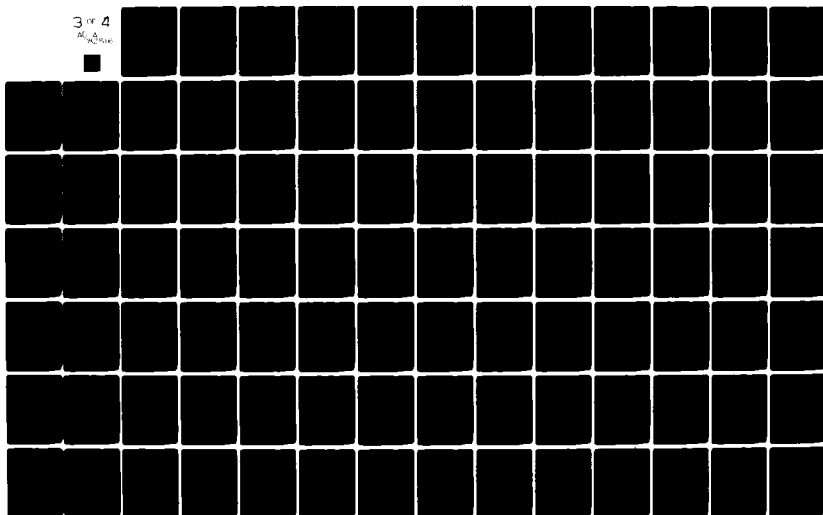
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DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Master Protocol for Phase II Drug Studies in Treatment of
Advanced, Recurrent Pelvic Malignancies.

WORK UNIT NO.: GOG 26

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

This protocol constitutes a Phase II design outlining the procedures that will be performed to screen for activity of new agents or drug combinations in patients with advanced recurrent pelvic malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

TECHNICAL APPROACH

This is a study of multiple chemotherapeutic agents. Therapy will follow the schema outlined in the study protocol. Agents to be used in this study include: Piperazinedione, Cis-Platinum, VP-16, Galacticol, Baker's Antifol, ICRF-159, Maytansine, m-AMSA and Yoshi 864.

PROGRESS

Results of this study will be used to determine the future role of the chemotherapeutic agent used in the treatment of gynecologic cancer either alone or in combination with other drugs.

Status: Ongoing.

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Melphalan, 5-FU, and Megace vs Adriamycin, Cytosan, 5-FU and Megace in the Treatment of Patients with Primary Stage III, Primary Stage IV, Recurrent or Residual Endometrial Carcinoma, Phase III.

WORK UNIT NO.: GOG 28

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of multi-drug preparations and to see if one of two programs previously shown to be effective by pilot studies is superior.

TECHNICAL APPROACH

Patient Eligibility: All patients with primary Stage III, primary Stage IV, recurrent or residual endometrial adenocarcinoma, adenocanthoma or adenosquamous cancer whose potential for cure by radiation therapy or surgery alone or in combination is very poor and who have received no prior chemotherapy other than progestins are eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

There is no significant difference in either response duration or time to response or for survival and progression-free interval between the two treatment regimens.

Status: Ongoing.

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Pelvic and Abdominal Radiation Therapy vs Pelvic Radiation and Melphalan vs Melphalan Alone in Stage II Carcinoma of the Ovary, Phase III.

WORK UNIT NO.: GOG 29

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the duration of relapse-free survival obtained by pelvic and abdominal radiation.
2. To determine the duration of relapse-free survival obtained by pelvic radiation and chemotherapy.
3. To determine the duration of relapse-free survival obtained by chemotherapy alone.
4. To study the influence of various forms of treatment, and of tumor differentiation upon patterns of relapse and recurrence; local, nodal, abdominal, diaphragmatic and distant disease.

TECHNICAL APPROACH

Patient Eligibility: All patients must have had an adequate surgical staging. At the time of surgical staging (restaging), the disease stage must be Stage IIa, IIb, or IIc. Patients must have a histopathologic diagnosis of ovarian cancer of one of the following types: serous, mucinous, endometrioid, clear cell, or undifferentiated.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study, and it is too early to report any meaningful results.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Local Excision vs Cryosurgery in Patients with Limited Grade 1, 2, or 3 Cervical Intraepithelial Neoplasia.

WORK UNIT NO.: GOG 31

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate and compare the immediate and long-term effectiveness of outpatient cryosurgery and outpatient local excision in the treatment of limited cervical intraepithelial neoplasia Grade 1, 2 or 3, in a randomized prospective study.

TECHNICAL APPROACH

Patient Eligibility: All patients must have a tissue diagnosis of cervical intraepithelial neoplasia within six weeks prior to randomization in the study. All patients must have a lesion which can be completely delineated through the colposcope. Only patients with the following histologic diagnosis will be eligible: mild dysplasia, moderate dysplasia, severe dysplasia, and carcinoma in situ.

Therapy and randomization will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Surgical Conization vs Cryosurgery
in Patients with Extensive Grade 3 Cervical Intraepithelial
Neoplasia.

WORK UNIT NO.: GOG 32

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate and compare the immediate and long-term effectiveness of outpatient cryosurgery to the standard cold-knife conization in the treatment of extensive cervical intraepithelial neoplasia grade 3 in a randomized, prospective study.

TECHNICAL APPROACH

Patient Eligibility: All patients must have a diagnosis of cervical intraepithelial neoplasia within six weeks prior to randomization in the study. All patients must have a lesion which can be completely delineated through the colposcope. The lesion should involve at least two quadrants of the portio. Only patients with the following histologic diagnosis will be eligible: severe dysplasia and carcinoma in situ.

Randomization and therapy will follow the schema outlined in the study protocol. ...

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Clinical-Pathologic Study of Stage I and II Carcinoma of the Endometrium.

WORK UNIT NO.: GOG 33

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS

OBJECTIVES

To determine the incidence of pelvic and aortic lymph node metastases and the relationship of these node metastases to other important prognostic factors.

TECHNICAL APPROACH

Patient Eligibility: All patients with histologically proven endometrial carcinoma clinical FIGO Stage I and II who are medically suitable for hysterectomy and lymphadenectomy are eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Study of Adriamycin as an Adjuvant After Surgery and Radiation Therapy in Patients with High Risk Endometrial Carcinoma Stage I and Occult Stage II.

WORK UNIT NO.: GOG 34

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study differences in morbidity and patient survival as functions of various tumor growth patterns as well as treatments.

TECHNICAL APPROACH

Patient Eligibility: All patients with primary, previously untreated, histologically confirmed invasive carcinoma of the endometrium Stage I, and Stage II occult, all grades, with one or more of the following high risk criteria are acceptable: (1) all lesions with equal to or greater than $\frac{1}{2}$ myometrial involvement; (2) positive pelvic and/or para-aortic nodes; (3) microscopic evidence of cervical involvement but no gross clinical involvement of the cervix. The following types of histologically confirmed uterine carcinoma are eligible: adenocarcinoma, adenoacanthoma, adenosquamous carcinoma.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study, and it is too early to report any meaningful progress.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Surgical-Pathologic Study of Women with Squamous Cell Carcinoma of the Vulva.

WORK UNIT NO.: GOG 36

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine validity of current FIGO staging to the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histologic grade, and site and number of positive lymph nodes in Stage I-IV carcinoma of the vulva.
2. To rapidly accumulate prospectively significant surgical pathologic data for development of further protocols for subsets of disease identified.
3. To determine morbidity of primary radical surgical therapy.

TECHNICAL APPROACH

Patient Eligibility: All patients with primary, previously untreated histologically confirmed invasive squamous cell carcinoma of the vulva clinically determined to be Stage I through IV.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Randomized Study of Radiation Therapy vs Pelvic Node Resection
for Patients with Invasive Squamous Cell Carcinoma of the Vulva
Having Positive Groin Nodes.

WORK UNIT NO.: GOG 37

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the benefit and morbidity of adding adjunctive radiation therapy to pelvis and groin for patients with positive groin nodes at radical vulvectomy and bilateral groin dissection.

TECHNICAL APPROACH

Patient Eligibility: All patients with primary, previously untreated, histologically confirmed invasive squamous cell carcinoma of the vulva such that radical vulvectomy suffices to remove all of the local lesion and whose surgery revealed that there were nodes in the groin on one or both sides containing metastatic carcinoma.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Clinical-Pathologic Study of Stage I and II Uterine Sarcomas.

WORK UNIT NO.: GOG 40

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the incidence of pelvic and aortic lymph node metastases associated with Stage I and II uterine sarcomas, the relationship of these node metastases to other important prognostic factors such as mitotic index of the tumor, and the complication rate of the procedures.

TECHNICAL APPROACH

Patient Eligibility: All patients with histologically proven uterine sarcoma clinical Stage I and II who are medically suitable for hysterectomy and lymphadenectomy are eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Surgical Staging of Ovarian Carcinoma.

WORK UNIT NO.: GOG 41

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the spread of ovarian carcinoma in intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy.
2. To establish a surgical protocol for patients entered into GOG ovarian cancer treatment protocols.
3. To determine the complication rate of the procedures.

TECHNICAL APPROACH

Patient Eligibility: Patients with all histologic types of primary ovarian cancer are eligible, including epithelial tumors, germ cell tumors, stromal tumors, and all others. Patients must be entered within two weeks of the last surgery.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Recurrent or Advanced Uterine Sarcoma. A Randomized Comparison of Adriamycin vs Adriamycin and Cyclophosphamide, Phase III.

WORK UNIT NO.: GOG 42

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if Adriamycin alone is more effective than Adriamycin and Cyclophosphamide in producing responses in advanced or recurrent uterine sarcoma.
2. To determine the duration of response for each different treatment arm.

TECHNICAL APPROACH

Patient Eligibility: Patients with primary Stage III, primary Stage IV or recurrent uterine sarcoma are eligible. Both patients with measurable and non-measurable disease are eligible, but they will be analyzed separately. Patients with all cell types of uterine sarcoma are eligible.

Randomization and therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Cis-Platinum 50 mg/m² IV Every Three Weeks vs Cis-Platinum 100 mg/m² IV Every Three Weeks vs Cis-Platinum 20 mg/m² IV Daily X 5 Days Every Three Weeks in the Treatment of Patients with Advanced Carcinoma of the Cervix, Phase III.

WORK UNIT NO.: GOG 43

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To confirm the effectiveness of cis-diamminedichloroplatinum (DDP) in advanced and recurrent squamous cell carcinoma of the cervix no longer responding to radiation therapy or surgery.
2. To compare the frequency and duration of response, and adverse effects of DDP therapy using three different doses and treatment schedules.
3. To evaluate the roles of serial determination of serum carcinoembryonic antigen (CEA) levels in determining extent of disease, response to treatment, and in predicting treatment failure.

TECHNICAL APPROACH

Patient Eligibility: Patients who have histologically confirmed, locally advanced, recurrent, persistent, or metastatic squamous cell carcinoma of the cervix which is resistant to curative treatment with surgery or radiotherapy. All patients must have lesions which are measurable or evaluable by physical examination. Patients will have recovered from effects of recent surgery or radiotherapy, and will be free of clinically significant infection.

Randomization and therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Adjuvant Vincristine, Dactinomycin, and Cyclophosphamide Therapy in Malignant Germ Cell Tumors of the Ovary After Resection of All Gross Tumor, Phase III.

WORK UNIT NO.: GOG 44

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To evaluate the effect of combined prophylactic vincristine, dactinomycin, and cyclophosphamide chemotherapy in patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (Grades 2 and 3), choriocarcinoma, and malignant mixed germ cell tumors of the ovary, Stages I and II after total removal of all gross tumor.
2. To evaluate the role of serum markers, especially alpha-fetoprotein (AFP) and human chorionic gonadotropin (beta HCG), when these are present, in predicting response and relapse.
3. To determine the role of restaging laparotomy in determining response, predicting relapse and planning further therapy.

TECHNICAL APPROACH

Patient Eligibility: Patients with histologically confirmed malignant germ cell tumors of the ovary, Stages I or II, if previously untreated and completely resected, excluding patients with pure dysgerminoma unless classified as anaplastic, are eligible. Patients with grade 2 or 3 immature teratoma are also eligible. Patients with early Stage III disease will be accepted if all gross tumor is resected.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Vinblastine, Bleomycin, and Cis-Platinum in Stage III and IV and Recurrent Malignant Germ Cell Tumors of the Ovary, Phase III.

WORK UNIT NO.: GOG 45

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To evaluate the effect of four cycles of combined Vinblastine, Bleomycin and Cis-Platinum (VBP) chemotherapy in the management of patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (all grades), choriocarcinoma, and malignant mixed germ cell tumors of the ovary with advanced or recurrent disease, incompletely resected.
2. To evaluate the role of serum markers, especially alpha-fetoprotein (AFP) and human chorionic gonadotropin (beta-HCG), when these are present, in predicting response and relapse.
3. To determine the role of restaging laparotomy in patients in clinical remission, in assessing completeness of response, and in planning further therapy.
4. To evaluate and compare the effect of Vincristine, Dactinomycin and Cyclophosphamide (VAC) chemotherapy in patients found to have persistent disease at the time of restaging laparotomy.
5. To determine the need for maintenance Vinblastine therapy in patients found free of disease at restaging laparotomy.

TECHNICAL APPROACH

Patient Eligibility: Patients with histologically confirmed malignant germ cell tumors of the ovary with advanced (Stage III-IV) or recurrent disease, incompletely resected, excluding patients with pure dysgerminoma (mature or anaplastic), are eligible. Patients with incompletely resected Stage II disease and patients previously treated with Vincristine, Dactinomycin and Cyclophosphamide are also eligible.

Therapy will follow the schema outlined in the study protocol.

GOG 45 (Continued)

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparison of Melphalan vs Intraperitoneal Chromic Phosphate in the Treatment of Women with Stage I (Exclusive of Stage IA(1) G1 and IB(1) G1) Epithelial Carcinoma of the Ovary, Phase III.

WORK UNIT NO.: GOG 46

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the relative effectiveness of Melphalan vs. intraperitoneal Chromic Phosphate as adjuvant therapy in Stage I exclusive of Stage IA (1) G1 and Stage IB (1) G1 epithelial cancers of the ovary in a randomized prospective study.

TECHNICAL APPROACH

Patient Eligibility: Patients with surgical Stage IA (1) G2, G3; IA (11); IB (1) G2, G3; IB (11), and IC epithelial cancer of the ovary who have undergone optimal staging described in GOG 41 are eligible.

Randomization and therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ovarian Cancer Study Group Protocol for Selected Stage IA1 -
IB1 Ovarian Cancer (Well and Moderately Differentiated).

WORK UNIT NO.: 7601

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To define the natural history (relapse rate, relapse site, relapse free survival) of patients treated by surgery alone.
2. To determine whether prophylactic, adjuvant chemotherapy with melphalan alters the natural history.
3. To study the effect of various potential prognostic factors (stratification factors) on the natural history of patients treated by each form of therapy.
4. To determine the patterns of relapse for each form of therapy.
5. To establish the value of various staging parameters on the stage of disease and its natural history.

TECHNICAL APPROACH

Patient Eligibility: All patients must have a histopathologic diagnosis of common epithelial ovarian cancer of one of the following types: serous, mucinous, and those listed in Appendix I of the protocol. After definitive staging procedures, the patient is a selective Stage I-A1 or I-B1 (Stage I-C) excluded, and whose histological grade is well or moderately differentiated.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ovarian Cancer Study Group Protocol for All Stage IC and II
(A,B,C) and Selected Stage IAii and IBii Ovarian Cancer.

WORK UNIT NO.: 7602

PRINCIPAL INVESTIGATOR: Milton H. Leman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To define the natural history (relapse rate, relapse sites, relapse free survival, regression rate, duration of regression) of patients treated by surgery plus either chemotherapy or chemotherapy plus radiation therapy.
2. To study the effect of various potential prognostic factors (stratification factors) on the natural history of patients treated by each form of therapy.
3. To determine the patterns of relapse for each form of therapy.
4. To establish the value of various staging parameters on the stage of disease and its natural history.

TECHNICAL APPROACH

Patient Eligibility: All patients must have a histopathologic diagnosis of common epithelial ovarian cancer of one of the following types: serous, mucinous or one of the types identified in Appendix I of the study protocol. After a definitive staging procedure, if the patient is Stage II-A, II-B, II-C, I-Aii, I-Bii, or I-Ai or I-Bi with poorly differentiated tumors, she is eligible for this study. The patient must have had no previous treatment except surgical therapy.

Randomization and therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

APPENDIX C

Southwest Oncology Group

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adjuvant Chemotherapy for Patients with Locally Advanced
Adenocarcinoma of the Large Bowel.

WORK UNIT NO.: SWOG 7510

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To determine the effectiveness of the combination of MeCCNU + 5-FU as
adjuvant chemotherapy.

To judge whether oral BCG adds to effectiveness.

TECHNICAL APPROACH

Patients with histologically proven Duke-C adenocarcinoma of the large
bowel with no proven residua or metastatic disease and no prior chemo-
therapy or radiotherapy are eligible for entry into this protocol.

Treatment will conform with the schema outlined in the study protocol.

PROGRESS

This study was designed to compare 5-FU + MeCCNU vs 5-FU + MeCCNU +
BCG with respect to disease-free survival. Subsequently the protocol
was amended to add a third control arm of patients who would receive
no further treatment beyond the initial surgery.

The disease-free interval of pre-amendment patients receiving chemo-
therapy is not at all significantly different than for those patients
receiving chemoimmunotherapy. Likewise for post-amendment patients,

SWOG 7510 (Continued)

either of these two arms appears to be superior to the control arm (delayed therapy) based on preliminary data. More toxicity (primarily thrombocytopenia) has been observed on the chemotherapy arm as compared to the chemoimmunotherapy arm. For preamendment patients, the risk of disease recurrence appears to be highest at approximately six months and again at approximately one year after the initial surgery.

So as to accrue more patients, the study remains open.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy with or without Immunotherapy in
High Risk Melanoma Patients: An Adjuvant Study.

WORK UNIT NO.: SWOG 7521

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of BHD in preventing recurrence of disease and prolonging survival of patients who have received definitive surgical treatment for their primary lesions.
2. To determine the efficacy of BHD + BCG in preventing metastases and prolonging the disease-free interval.
3. To determine the immunocompetence of these patients.

TECHNICAL APPROACH

Eligibility: All patients with histologically confirmed diagnosis of malignant melanoma previously untreated with chemotherapy or radiotherapy, who are within 4 weeks of surgical excision of active disease.

PROGRESS

Accrual is good in the Class I portion of this study. There are 37 evaluable patients on the arm receiving immediate treatment, and 39 evaluable patients on the arm receiving delayed treatment. There have been 9 relapses in this group, 6 of them in the delayed treatment arm. This portion of the study will remain open.

SWOG 7521 (Continued)

In Class II of this study, there have been 117 patients registered on the BHD arm of the study, with 27 relapses, and 113 patients registered on the BHD + BCG arm, with 31 relapses. There is no statistically significant difference between the two limbs, although there is more toxicity reported in the BHD alone arm; also in this arm, the disease free interval is less than the BHD + BCG arm. There seems to be doubt as to whether BCG is adding anything to the study. Since there has been adequate registration in Class II of this study, this portion was closed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy, Splenectomy with or without Immunotherapy in
the Treatment of Chronic Myelogenous Leukemia.

WORK UNIT NO.: SWOG 7522

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To study the effects of chemotherapy, splenectomy and/or immunotherapy
on leukemic cytogenetics, immune status, appearance of blastic trans-
formation, and any influence in overall survival.

TECHNICAL APPROACH

Eligibility: All patients with confirmed diagnosis of benign phase
CML not previously treated with any of the agents used in this study.

Treatment will conform with the schema outlined in the study protocol.

PROGRESS

This study remains open for patient registration.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy in Stages III and IV Ovarian and Endometrial Cancer.

WORK UNIT NO.: SWOG 7524

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness of chemotherapy alone vs. chemo-immunotherapy for remission induction in Stages III and IV ovarian and endometrial carcinoma.
2. To test the effectiveness of chemotherapy plus immunotherapy vs. chemotherapy in maintaining complete remissions.
3. To test effectiveness of continued chemotherapy plus immunotherapy vs. chemotherapy in inducing complete remission or maintain partial remissions in patients with occult disease at restaging or in patients achieving only partial remission during 12 months induction therapy.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed ovarian carcinoma or endometrial carcinoma Stage III or IV with no prior chemotherapy or concurrent progestational agent therapy are eligible. Adenocarcinoma of cervix and germ cell of the ovary are eligible.

Therapy will be according to the schema outlined in the study protocol.

PROGRESS

Ovarian Carcinoma: After three years of observation, the data collected from patients registered on this protocol have shown statistically significant evidence that BCG added to the standard adriamycin-cyclophosphamide regimen increases percentage of complete responses plus partial responses overall survival duration. These results cannot be explained on the basis of an imbalance of prognostic factors between

SWOG 7524 (Continued)

the two groups of patients. A similar distribution existed between the two study arms with respect to Stage IV disease, bulky tumor masses, types of surgical procedures, performance status, prior radiation therapy exposure, and administered drug dosages for each course of therapy. Although pathologic review by a panel of SWOG pathologists is not complete, there appears an even distribution of histologic cell types between the two treatment groups and an extremely high percentage of patients with high grade tumors. Final validation of adriamycin-cyclophosphamide + BCG as superior therapy will have to await completion of pathology review and further patient follow-up.

Endometrial Carcinoma: The data for the endometrial carcinoma study continue to look promising. 43% of the A-C + BCG patients had documented partial remission, whereas 38% of the A-C patients had partial remissions. An additional 7% of patients on A-C + BCG had 19% on A-C had objective tumor reductions on therapy. The median duration of response was 5 months for both groups of patients.

The median duration of survival for A-C + BCG patients was 17 months compared to 7.5 months for A-C patients. If the present survival data are documented through another year of patient accrual, BCG may prove to be an important new drug in the treatment of endometrial cancer.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Patients for Early Testicular Cancer with Irradiation and Chemotherapy with Vinblastine and Bleomycin.

WORK UNIT NO.: SWOG 7525

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if a combination of irradiation and chemotherapy can improve the 2 year disease free interval and 5 year survival in certain morphologic subtypes of Ib and II nonseminomatous testicular tumors.
2. To determine which sequence of irradiation and chemotherapy more favorably influences remission and maintenance, survival and possibly cure. In part, this will be done by compression of the AFIP classification into a more therapeutically workable classification which excludes pure seminomas and choriocarcinomas.

TECHNICAL APPROACH

Eligibility: Previously untreated patients with histologically proven Stage IB and II pure embryonal, pure teratocarcinomas, mixed cell types with seminomatous elements.

Therapy will be administered according to the schema outlined in the study protocol.

PROGRESS

This study is replaced by the Intergroup Testicular Study.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Immune Evaluation of Lymphoma in Unmaintained Remission

WORK UNIT NO.: SWOG 7580

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the immune status of patients with lymphoma who have been successfully treated and are in remission without therapy.
2. To correlate the presence of immune deficits with histologic type of lymphoma, pathologic stage, types of therapy and interval since therapy.
3. To correlate the immunologic profile with long term follow-up of patients in terms of disease relapse, second malignancy, and duration of survival.

TECHNICAL APPROACH

Eligibility: Any patient with histologically proven Hodgkin's or non-Hodgkin's lymphoma, who has completed therapy and has had at least 3 months of unmaintained remission.

Evaluation will be carried out in accordance with the schema outlined in the study protocol.

PROGRESS

Fifty-eight cases of Hodgkin's disease, 25 of non-Hodgkin's disease and 19 normals were evaluated. The incidence of anergy was about 10% in Hodgkin's disease. Two-thirds of the patients had an inability to respond to DNCB and KLH. All responded to PHA. The disease-free interval ranged from 1-5 years in the cases analyzed.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Schedule of Activity of 5-Azacytidine in Acute Leukemia.

WORK UNIT NO.: SWOG 7603

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To compare the activity and toxicity of single dose vs. continuous 5-day infusions of 5-Azacytidine in patients with acute leukemia.

TECHNICAL APPROACH

Eligibility: Patients with bone marrow diagnosis of acute leukemia who are ineligible for or who have relapsed on a leukemia protocol of higher priority.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Among 81 evaluable patients, there were five complete responses and two partial responses. No responses were seen with 750 mg/M². There was one complete response and one partial response among 25 evaluable patients treated with 300 mg/M²/day x 5 days. There have been no responses seen in the four patients registered on the 10-day regimen. Early deaths totaled 22.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Disseminated Testicular Cancer with Vinblastine, Bleomycin, Cis-Platinum, Chlorambucil and Actinomycin-D.

WORK UNIT NO.: SWOG 7610

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the effectiveness of Vinblastine, Bleomycin, and Cis-Platinum in remission induction.
2. To determine the duration of remission with a maintenance combination of Chlorambucil and Actinomycin-D alternating with Vinblastine.

TECHNICAL APPROACH

Eligibility: Patients of an age with Stage III metastatic testicular carcinoma who have not been previously treated with any of the selected agents.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

The complete response rate for all patients was 52%. Those with adequate marrow status had a higher complete response rate (54%) than those with inadequate marrow status (33%). This was not a statistically significant difference ($p = .171$).

The survival rate at six months was 87% and at 12 months was 75%. Median survival was greater than 120 weeks.

Relapse-free rates at six months were 87% after complete response and 46% after partial response. 82% were relapse-free at 12 months

SWOG 7610 (Continued)

after complete response. Median remission duration after partial response was four months and was greater than 12 months after complete response.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-Platinum for Refractory Sarcomas.

WORK UNIT NO.: SWOG 7611

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of Cis-Platinum in the treatment of patients with advanced sarcomas refractory to Adriamycin combinations.

TECHNICAL APPROACH

Eligibility: Patients with a biopsy confirmed diagnosis of soft tissue or bony sarcoma and not eligible for a higher priority protocol. Patients must have measurable disease.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Very little activity of Cis-Platinum was noted for refractory sarcomas. One complete remission was reported in mesothelioma.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Preoperative Adjuvant Therapy in Rectal Carcinoma.

WORK UNIT NO.: SWOG 7618

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if adjuvant preoperative radiotherapy and chemotherapy will yield a higher incidence than expected of Duke A lesions in a high risk group.
2. To determine the survival of patients with and without regional node metastases.

TECHNICAL APPROACH

Eligibility: Patients with carcinoma of the rectum judged by the surgeon to have clinically resectable disease by abdominoperineal resection.

Therapy will conform with the schema outlined in the study protocol.

PROGRESS

The study was closed because of inadequate patient accrual.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy or Chemotherapy + Immunotherapy Following Initial Surgery and/or Radiotherapy for Treatment of Early Squamous Cell Carcinoma of the Head and Neck.

WORK UNIT NO.: SWOG 7620

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if the disease-free interval and survival of patients in high risk categories of squamous head and neck cancer can be improved by adjuvant chemotherapy or chemimmunotherapy after initial surgery, radiotherapy or combination approach have resulted in no clinically evident disease.
2. To accumulate immunologic data in treated and untreated patients with this malignancy.

TECHNICAL APPROACH

Eligibility: Patients with no evidence of clinical disease three months after completion of surgery or irradiation.

Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

This study was closed because of inadequate patient accrual.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adriamycin vs. Adriamycin plus Cis-Platinum in Transitional Cell Bladder Carcinoma.

WORK UNIT NO.: SWOG 7624

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D, MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To compare the efficacy of Adriamycin vs. Adriamycin + Cis-Platinum in recurrent or disseminated transitional cell bladder carcinoma.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven T₄ transitional cell bladder carcinoma, T₃ if there is a general contraindication to radical surgery; recurrent or residual cases after surgery, radiotherapy or both; and M₁ cases of liver, osseous, pulmonary or other metastasis.

Randomization and therapy will follow the schema outlined in the study protocol.

PROGRESS

Response from Cis-Platinum alone was not statistically better than the combination Adriamycin + Cis-Platinum, and both arms had lower response rates than others achieved. 40% of evaluable patients had stable disease on each arm.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Chemotherapy for Advanced Sarcoma of the Bone and Mesothelioma Utilizing Rubidazone and DTIC.

WORK UNIT NO.: SWOG 7625

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy in terms of rate of response of combination chemotherapy with the 2-drug regimen, RubiDIC (Rubidazone + DIC) in patients with metastatic sarcomas of bone and mesothelioma.
2. To determine the duration of remission and survival pattern of patients on this study and compare them with that of patients with metastatic bone sarcomas and mesothelioma on previous SWOG or M.D. Anderson Hospital protocols using Adriamycin containing regimens.
3. To determine the toxicity of the regimen especially with regard to cardiac toxicity.

TECHNICAL APPROACH

Eligibility: Patients with a biopsy-confirmed diagnosis of bone sarcoma or mesothelioma with measurable metastases who have already received appropriate surgical therapy and who have not received prior Adriamycin, Daunorubicin, Rubidazone, DIC or BIC are eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

In osteogenic sarcoma, only 15 patients were registered, with only 10 fully evaluable patients and no responders.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: ROAP Induction of Chemotherapy for Acute Leukemia Patients
Over the Age of 50.

WORK UNIT NO.: SMOG 7626

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of the 4-drug combination chemotherapy regimen ROAP (rubidazone, vincristine, arabinosyl cytosine and prednisone) in remission induction chemotherapy in patients with acute leukemia over the age of 50.
2. To determine the toxicity of the regimen.

TECHNICAL APPROACH

Eligibility: All patients age 50 or greater with a diagnosis of acute leukemia who have received no extensive prior therapy (defined as one course or less of any other chemotherapeutic agent or combination of agents) will be eligible for this study. The diagnosis of acute leukemia will be made on bone marrow smear clot section and/or biopsy. An absolute infiltrate of 50% leukemic cells or greater is required. Absolute infiltrate is defined as the total blast cell percentage multiplied by the bone marrow cellularity percentage divided by 100.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

For patients 50 to 60 years of age, the complete remission rate on this study was superior to that for CIAL, while the reverse was true for patients under age 40. Consistent with what has been observed for response rate, survival on this study appears inferior to CIAL for patients under 50 and equal to or superior to CIAL for patients over age 40.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Chemotherapy/Radiotherapy/Immunotherapy for Oat Cell Cancer of the Lung.

WORK UNIT NO. SWOG 7628

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To use combination chemotherapy, local radiotherapy, and maintenance chemotherapy or chemoimmunotherapy in the treatment of oat cell carcinoma of the lung in order to improve the quality and duration of survival.

TECHNICAL APPROACH

Eligibility: Histologically proven diagnosis of oat cell carcinoma or small cell undifferentiated carcinoma of the lung.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Response rates on this study did not differ significantly by type of chemotherapy. This was true for all patients combined, for limited disease patients only, and for extensive disease patients only. Furthermore, BCG did not significantly improve response rates compared to patients not receiving BCG.

Toxicity was generally comparable on all treatment arms except CHO + BCG. Here, there was evidence of the overall worst degree of toxicity

SWOG 7628 (Continued)

to be significantly higher on this particular treatment arm. This seemed to relate primarily to comparison of granulocytopenia incidence or thrombocytopenic incidence by treatment.

Overall, length of survival did not differ significantly by treatment. Limited disease patients survived much longer than extensive disease patients. Limited disease patients did not survive differently by type of chemotherapy given, nor by presence or absence of BCG therapy. Concerning radiotherapy evaluations, the survival was not at all different between patients with major XRT protocol variations versus those with only minor XRT variations or no variations. Intended XRT dose appeared to relate to survival. Patients receiving the additional 1500 rads as a second course survived significantly longer.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-Platinum in Refractory Epidermoid Carcinoma of the Head and Neck.

WORK UNIT NO.: SWOG 7629

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy and toxicity of Cis-Platinum and mannitol in the treatment of refractory epidermoid head and neck carcinoma.

TECHNICAL APPROACH

Eligibility: Patients with epidermoid carcinoma of the head and neck region with measurable disease, who are not eligible for protocols of higher priority.

Therapy is administered according to the schema outlined in the study protocol.

PROGRES

The use of Cis-Platinum, the IV bolus, appeared to be more effective for induction maintenance. Median duration of complete regressions was 8+ months and for partial responses was 2 months.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Advanced Prostatic Cancer.

WORK UNIT NO.: SWOG 7630

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare rate of response of Hydroxyurea versus Adriamycin + Cytosan.
2. To compare the duration of survival in patients with nonmeasurable disease.
3. To estimate the response rate to each crossover regimen.

TEHCNIAL APPROACH

Eligibility: All patients with advanced Stage D prostatic cancer who have not received Hydroxyurea, Adriamycin or Cytosan.

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

To date, 104 patients have been entered on the study. More patients with measurable disease are needed before any meaningful results can be reported.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Modality for Recurrent Breast Cancer.

WORK UNIT NO.: SWOG 7632

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal-chemotherapeutic approach.
2. To determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery.
3. To correlate hormonal manipulations with estrogen and progesterone receptors where possible.

TECHNICAL APPROACH

Eligibility: Only patients who have been surgically and/or radiotherapeutically treated with the intent to cure their primary disease are eligible. In addition, patients with castration are eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

A similar response rate of approximately 30% in all ER+ and ER unknown patients was noted. Four of 32 patients responded to castration + continued Tamoxifen; 2 of 32 patients are stable. Tamoxifen toxicity was demonstrated in 2/100 patients with flair-up. Patients reaching chemotherapy stage had 61% response rate.

ER = Estrogen Receptor.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Rubidazone in Adults with Previously Treated Acute Leukemia
and Patients with CML Blast Transformation.

WORK UNIT NO.: SWOG 7633

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of Rubidazone in adult patients with previously treated acute leukemia and in patients with CML blast transformation.
2. To determine the toxicity of the drug in the above patients with special reference to patients having prior therapy with Adriamycin.

TECHNICAL APPROACH

Eligibility: Adult patients with acute leukemia having had prior chemotherapy and patients with CMLBT will be eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

The results of this study are significantly less positive than the M.D. Anderson Study. In acute leukemia patients, the complete remission rate was 21% (21/71) in good risk patients, and the partial remission rate was 10% (7/71). There were no complete or partial responses in the 16 poor risk patients, and the difference in complete remission rate between good and poor risk patients was suggestive ($p = 0.98$, two-sided test). If one tested the hypothesis that good risk patients had a higher response rate than poor risk

SWOG 7633 (Continued)

patients, then the result would be statistically significant at the .05 level ($p = .05$, one-sided test). The median survival time was 12 weeks for good risk patients versus 5 weeks for poor risk patients.

Among the patients with CML blast crisis, there were no complete remissions in the 24 patients evaluated for remission status, and there was one partial remission in a 53-year-old male who died after 22 weeks. The median survival time among CML patients was 7 weeks.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of MeCCNU plus BTGdR and Mitomycin-C plus BTGdR
in the Treatment of Refractory Disseminated Colorectal
Carcinoma.

WORK UNIT NO. SWOG 7634

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To evaluate the effectiveness of MeCCNU plus BTGdR vs. Mitomycin-C
plus BTGdR for remission induction or for relapsing patients from
prior chemotherapy.

TECHNICAL APPROACH

Eligibility: All patients with disseminated colorectal carcinoma who
are not eligible for studies of higher priority.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

No significant differences in PR rates by treatment have been observed
in any of the three major patient subgroups defined by prior chemo-
therapy. There is some statistical evidence that SD and/or PR + SD
rates do differ significantly by treatment. These differences favor
 β + MeCCNU in patients with prior chemotherapy, but they favor β +
Mito-C in patients with no prior chemotherapy.

There is somewhat more leukopenia on the β + Mito-C arm and somewhat
more nausea/vomiting on the MeCCNU arm. Patients on the β + Mito-C

SWOG 7634 (Continued)

treatment arm have consistently more toxicity if they have had the more extensive prior chemotherapy. This is true also on the β + MeCCNU treatment arm, but to a lesser extent.

Length of survival does not differ at all significantly by treatment for either the randomized or the non-randomized patients. Survival is significantly related to amount of prior chemotherapy in the following order of decreasingly favorable prognosis: none, pyrimidine only, pyrimidine + Mito-C or MeCCNU. Since the post-amendment patients have less follow-up time than the pre-amendment patients, this survival difference may be only a transient one.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Modality Treatment for Limited Squamous Carcinoma of the Lung.

WORK UNIT NO.: SWOG 7635

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether chemotherapy with Adriamycin and/or immunotherapy with Levamisole improve median survival of split-course radiotherapy used alone in the treatment of patients with limited extent squamous bronchogenic carcinoma.
2. To determine the qualitative and quantitative toxicity of each treatment regimen.

TECHNICAL APPROACH

Eligibility: All patients with a histologically confirmed diagnosis of limited squamous carcinoma of the lung are eligible provided they have received no previous chemotherapy or radiation therapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

No significant differences have been observed by treatment with respect to either response rates, toxicity, or length of survival. One possible exception to this might be the mildly significantly higher response rate on XRT-Adriamycin as compared to XRT-Levamisole-Adriamycin. This is the first full analysis of data on this protocol, and therefore, results are of course preliminary at best.

SWOG 7635 (Continued)

At the present time, Levamisole does not confer any therapeutic advantage at all; in fact, patients not receiving Levamisole have higher response rates and longer survival, although neither of those differences is significant. Likewise, patients receiving adriamycin do not benefit compared to those not receiving it. The Adriamycin patients have a slightly lower response rate, and slightly inferior survival, although here again these differences are not significant.

Toxicity has been mild overall on all four treatment arms, although one patient did experience fatal thrombocytopenia. It is recommended that this study continue, although careful consideration should be given to the implications of the present accrual rate.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adriamycin, Mitomycin-C, and 5-FU in Gastric Carcinoma.

WORK UNIT NO.: SWOG 7639

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine and to document both the response rates and the toxicities of two different combinations of Adriamycin, Mitomycin-C and 5-Fluorouracil in the management of surgically incurable adenocarcinoma of the stomach.
2. To compare the effectiveness of these two regimens.

TECHNICAL APPROACH

Eligibility: Patients must have unresectable gastric adenocarcinoma and an objectively measurable lesion. No prior exposure is permitted to Adriamycin, Daunomycin, Mitomycin-C or Porfiromycin. If previous chemotherapy has been given, full recovery from its effects must have been achieved before this regimen is started.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Simultaneous FAM appears to give higher response rates than sequential FAM, although the statistical evidence supporting this is only mildly significant. Furthermore, this is not at all the case in patients with prior 5-FU chemotherapy. Toxicity on the two treatment arms was fairly comparable, and adequate to assure that patients were not undertreated. Survival on simultaneous FAM is slightly longer, but not significantly so. Survival of measurable and non-measurable disease patients cannot

SWOG 7639 (Continued)

be distinguished statistically. Responders survive significantly longer than non-responders. Patients without evidence of increasing disease also survive much longer than patients with increasing disease. There is a slight but nonsignificant survival benefit for patients who experience severe or worse grade of hematologic toxicity compared to those who do not.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: CIA vs. Ifosfamide Alone in Extensive Squamous Lung Cancer.

WORK UNIT NO.: SWOG 7701

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if Ifosfamide, Adriamycin, CCNU is a more effective combination than Ifosfamide alone or in combination with Adriamycin in the treatment of patients with extensive non-oat cell carcinoma of the lung who are not eligible for curative radiotherapy.
2. To measure the relative efficacy of this regimen on survival.
3. To determine the qualitative and quantitative toxicity of the regimen.

TECHNICAL APPROACH

Eligibility: All patients with a histologically confirmed diagnosis of extensive non-oat cell carcinoma of the lung are eligible, provided they have received no previous chemotherapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Significant differences in response rates among the three treatment arms have been detected, but only because the 2-drug treatment arm has such a suspiciously lower response rate (7%) than the other two treatment arms (25-26%). They do not differ significantly by prior SRT status, nor by performance status.

Length of survival does not differ significantly by treatment.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Radiation Therapy in Combination with BCNU, DTIC or Procarbazine in Patients with Malignant Gliomas of the Brain.

WORK UNIT NO.: SWOG 7703

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To compare the effectiveness of radiation therapy plus BCNU, radiation therapy plus DTIC, and radiation therapy plus Procarbazine for remission induction, duration of remission, and survival in patients with malignant gliomas of the brain.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed primary central nervous tumors of the following histologic types are eligible: Astrocytoma, grades 3 and 4 (glioblastoma multiforme).

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Evaluation of response and duration of remission indicates that the complete remission rate was 22% (7/32) on Treatment 1, 20% (3/15) on Treatment 2, and 14% (4/29) on Treatment 3. There is no evidence of a statistically significant difference in complete remission rates among treatments. The complete + partial remission (CR+PR) rates in this analysis are 28% (9/32), 67% (1/15), and 38% (11/29), respectively on the three treatments. There is evidence of a statistically significant difference among complete + partial remission rates

SWOG 7703 (Continued)

($p = .04$), though this difference should be considered in the light of the survival data.

The median lengths of survival on the three treatments are 41, 36, and 47 weeks, respectively, and there is no evidence of statistically significant differences among treatments.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy/Immunotherapy for Multiple Myeloma.

WORK UNIT NO.: SWOG 7704

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness of three intermittent pulse chemotherapy combinations VMCP + VCAP vs. VMCP + VBAP vs. MP for induction of remission in previously untreated patients with multiple myeloma.
2. For patients proven to have at least a 75% tumor regression after induction, to compare the value of 12 months of chemoimmunotherapy maintenance VMCP + Levamisole in comparison to VMCP alone.
3. To establish baseline and serial data on immunologic status in these patient groups.

TECHNICAL APPROACH

Eligibility: All previously untreated patients with multiple myeloma (all stages) are eligible. Patients without prior cytotoxic chemotherapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

The frequency of response from Melphalan-Prednisone was less than from the more complex combinations, and the preliminary survival times from MP were shorter. These findings reaffirm the superiority of the more complex regimens in the initial treatment of multiple myeloma, in comparison with Melphalan-Prednisone. The Melphalan-Prednisone arm is closed as it remains inferior to the other two arms. Results on arm 1 and 2 are encouraging.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy for Stages III and IV Ovarian Carcinoma Resistant to Adriamycin-Cyclophosphamide or Single Alkylating Agent.

WORK UNIT NO.: SWOG 7706

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To use a combination of 5-FU, Hexamethylmelamine and Cis-Platinum in an attempt to induce complete and partial clinical remissions in patients with stages III and IV ovarian carcinoma who have failed to respond to or have relapsed following remission from Adriamycin-Cyclophosphamide therapy.
2. To use a combination of 5-FU, Hexamethylmelamine, Cis-Platinum and Adriamycin to induce complete and/or partial remissions in patients with stages III and IV ovarian carcinoma who have failed on or relapsed from previous alkylating agent therapy.

TECHNICAL APPROACH

Eligibility: Only patients with pathologic stages III or IV ovarian carcinoma who have failed on prior Adriamycin-Cyclophosphamide or alkylating agent therapy will be eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study shows that a relatively high objective response rate (i.e. 44%) can be achieved in alkylating resistant ovarian carcinoma patients using a 4-drug combination which includes Adriamycin, 5-FU, Hexamethylmelamine and Cis-Platinum. Patients with prior exposure to both an alkylating agent and Adriamycin had a very low response rate to the 3-drug combination. Adriamycin, used as a single agent

SWOG 7706 (Continued)

in the treatment of alkylating agent refractory ovarian carcinoma, has proven to be limited efficacy in inducing responses. A possible explanation for the high response rates achieved in patients with the 4-drug combination including Adriamycin, is the apparent therapeutic synergism between the drug and Cis-Platinum. The very low response rate to the 3-drug regimen is disturbing, especially since Hexamethylmelamine used as a single agent in higher daily dosage has been associated with 26-38% response rates in alkylator resistant ovarian carcinoma. By decreasing the dosage of this latter drug in order to fit it into a combination chemotherapy regimen, it is possible that its antitumor effects have been seriously impaired. By the same token, Cis-Platinum alone in low dosage (i.e. 50 mg/M² every 3 weeks) induced 6 partial responses in 19 patients and at very high dosage (i.e. 120 mg/M² every 3 weeks) induced 5 partial responses in 10 patients treated by Brucker et al. at Mt. Sinai Medical School. Judging from this data and the results of our study, one possible approach to combination chemotherapy in the treatment of Adriamycin-alkylating agent refractory ovarian cancer would be to combine high-dose Cis-platinum with daily high-dose Hexamethylmelamine.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Previously Treated Patients using VBAP, Phase II.

WORK UNIT NO.: SWOG 7707

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To evaluate the frequency and completeness of response with Vincristine, BCNU, Adriamycin and Prednisone combination (VBAP) chemotherapy in patients with malignant lymphoma (non-Hodgkin's disease and Hodgkin's disease) who have received prior therapy and are not eligible for higher priority studies.

TECHNICAL APPROACH

Only patients who had recurrent disease after extensive prior chemotherapy were eligible for this study.

Sixty-eight patients (41 men and 27 women, ages 20-74) received Vincristine 1 mg. IV, BCNU 30 mg/M² IV, Adriamycin 30 mg/M² IV, and Prednisone 100 mg daily x 4 days at 3 week intervals.

PROGRESS

Objective responses were noted in 6 (43%) of 14 patients with Hodgkin's disease and in 22 (41%) of 54 patients with non-Hodgkin's lymphoma. None of the 68 patients had received a nitrosourea previously, but 27 had received Adriamycin. Of the 54 patients with non-Hodgkin's lymphoma, similar response rates were seen with nodular and diffuse histologies (10 of 24 and 10 of 30, respectively). Twenty-four (92%) of 26 responders had previously shown a response to prior chemotherapy. Durations of response for the entire group ranged from 4 to

SWOG 7707 (Continued)

60+ weeks (median 39 weeks). The median duration of survival for all patients was 32 weeks. VBAP generally was very well tolerated with minimal nausea and only mild to moderate myelosuppression despite extensive prior chemotherapy. It is concluded that VBAP is effective, well tolerated, palliative chemotherapy for patients with refractory lymphoma.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemoimmunotherapy in Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 7713/14

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the effectiveness, in terms of rate of response to two chemoimmunotherapy regimens (CHOP + Levamisole vs. CHOP + Levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma.
2. For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with Levamisole vs. no maintenance therapy.
3. For patients with impaired cardiac function (not eligible for treatment with Adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with CHOP-Levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + Levamisole.
4. To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.
5. To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hemato-pathology review of diagnostic material from all cases.
6. To establish baseline and serial data on immunologic status in both chemoimmunotherapy groups.

TECHNICAL APPROACH

The patient must have the diagnosis of non-Hodgkin's lymphoma established by biopsy. All histologic types of non-Hodgkin's lymphoma,

SWOG 7713/14 (Continued)

according to the Rappaport classification will be eligible. Patients with chronic lymphocytic leukemia are ineligible.

PROGRESS

The induction arm complete response duration has shown a one-half year relapse free survival of 78% CHOP, 100% CHOP + Levamisole and 100% CHOP + Levamisole + BCG.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Tamoxifen in Renal Cell Carcinoma.

WORK UNIT NO.: SWOG 7716

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the response rate and survival in patients with disseminated renal cell carcinoma treated with Tamoxifen.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven disseminated renal cell carcinoma who have not received anti-estrogen agents before are eligible. Expected survival should be a minimum of 8 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Forty-nine patients have been evaluated for response and toxicity-- 38 males and 11 females with age range from 26 to 78 years. Two patients had partial remission (PR) (both males) while 14/49 (28%) experienced improvement or stabilization of their disease. No difference in response (PR + Improved + Stable) between the sexes was found. The median survival was better for responders (15.5 weeks) and for those with good initial performance status (16 weeks) than for patients with progressive disease or poor performance status

SWOG 7716 (Continued)

(8 and 6.5 weeks, respectively). No differences were found in response rate or survival between patients with previous hormonal and/or chemotherapy (22) and patients with no previous systemic therapy (27). Tamoxifen was well tolerated with minimal side effects. 3/49 had nausea and vomiting, 2/49 weakness, and 2/49 leukopenia with sweating, anorexia, flushing or abdominal cramps noted in one patient each. It was concluded that Tamoxifen 20 mg/day is well tolerated in patients with advanced renal carcinoma producing 32.6% partial, improved and stable disease. Tamoxifen may be recommended to be used in combination with other active therapeutic agent(s) for the treatment of patients with advanced renal cancer.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Management of Patients with a Metastatic Adenocarcinoma of Unknown Primary.

WORK UNIT NO.: SWOG 7717

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the yield of various diagnostic procedures in finding the site of tumor origin in patients who present with metastatic adenocarcinoma with no obvious primary source.
2. To compare the efficacy of combination chemotherapy using 5-FU, Adriamycin and Cytosin vs. 5-FU alone in the palliative management of patients with metastatic adenocarcinoma of unknown origin.
3. To assess the hematologic toxicity of the chemotherapy regimen on treated patients.

TECHNICAL APPROACH

Eligibility: Patients with metastatic adenocarcinoma with no obvious primary source are eligible for diagnostic evaluation. In addition they should meet the following criteria:

1. Should have histopathologic confirmation of their disease.
2. Patients must have measurable disease and an expected survival of 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Twenty-three patients are evaluable at this time. Eleven patients to date have been treated with the 3-drug combination therapy; of these two have attained partial response status.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Modality for Removable Lung Cancer.

WORK UNIT NO.: SWOG 7718

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine if immunotherapy in the form of Levamisole and post-operative intrapleural BCG prolongs the median disease-free interval and survival of resected (T_1 or T_2 , N_0 , M_0) non-small cell carcinoma of the lung.
2. To determine whether immunotherapy in the form of Levamisole and intrapleural BCG prolong the median disease-free interval and survival of non-small cell carcinoma of the lung (T_3 , N_{any} , M_0) or (T_{any} , N_1 , or N_2 , M_0) treated with resection and subsequent postoperative radiotherapy.

TECHNICAL APPROACH

Eligibility: Patient must have potentially resectable squamous, adeno or large cell carcinoma of the lung.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Patient accrual has been very slow. In addition, negative results from a study with similar design suggests an adverse effect of Levamisole.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Addition of CCP and Bleomycin to VBAP in Relapsing and Resistant Myeloma Patients, Phase II.

WORK UNIT NO.: SWOG 7719

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the frequency, degree and duration of response with Cis-Platinum (DDP) and Bleomycin (Bleo) added to Vincristine-BCNU-Adriamycin-Prednisone combination (VBAP) to combinations of Melphalan and/or Cyclophosphamide with Prednisone (M/C+P).
2. To compare results with previous SWOG trials of VBAP in such patients.

TECHNICAL APPROACH

Eligibility: Patients with the diagnosis of multiple myeloma who are no longer responding to or have not responded to Melphalan/Cyclophosphamide with Prednisone.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Among the low number of evaluable patients, responses have been noted only in relapsing patients, an experience similar to that from VBAP treatments on Protocol 7432.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Management of Oligoblastic Leukemia.

WORK UNIT NO.: SWOG 7720

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC, Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To collect data on the clinical course of patients with acute oligoblastic (smoldering) leukemia, a subgroup of acute leukemia patients who do not meet the requirements of the current Southwest Oncology Group chemotherapy protocol which requires greater than a 50% absolute leukemic infiltrate.
2. To compare the randomly assigned immuno-stimulant effect of levamisole on half this group of patients, as opposed to those receiving no specific treatment.
3. To maintain data on those patients in this group who subsequently attain a marrow status, which qualified them to transfer to active chemotherapy protocols.

TECHNICAL APPROACH

Eligibility: Any previously untreated patient with a diagnosis of acute non-lymphocytic leukemia (excluding blast crisis of CGL), whose absolute marrow blast cellularity is less than 50%, should be registered in this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Six patients have been entered on the study. It is too early for evaluation.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Diglycoaldehyde in Adult Acute Leukemia, Phase II Study.

WORK UNIT NO.: SWOG 7723

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the response of adult acute leukemia to diglycoaldehyde.
2. To study the toxicity of the drug.

TECHNICAL APPROACH

Eligibility: Patients with all cell types of acute leukemia will be eligible for the study. They will be in relapse after an initial response to other therapies or they may have failed to respond.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

The accrual rate on this study is somewhat slow with only 12 registrations. It is too early to report the results of treatment.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Diglycoaldehyde in Metastatic Malignant Melanoma, Phase II Study.

WORK UNIT NO.: SWOG 7724

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the response of metastatic malignant melanoma to diglycoaldehyde.
2. To study the toxicity of the drug.

TECHNICAL APPROACH

Eligibility: Patients with disseminated disease who have relapsed or are resistant to regimens in a higher priority will be eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Seven patients have been registered on this study. Of these, only one is fully evaluable. No responses have been seen.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: CMPF vs. CMPF + Levamisole for ER⁻ Patients with Breast Cancer.

WORK UNIT NO.: SWOG 7725

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the respective effects of Levamisole on the duration of response and survival of patients with advanced breast cancer concurrently treated with maintenance chemotherapy after a successful remission induction trial of continuous Cooper regimen.
2. To accumulate data on immunologic variables under the conditions of chemotherapy alone and combined chemotherapy and immunotherapy with Levamisole of advanced breast cancer.

TECHNICAL APPROACH

Eligibility: Only patients proven to be ER negative are eligible. Patients with measurable lesions and no previous experience of chemotherapy other than adjuvant chemotherapy. Life expectancy of 2 months is assumed.

Therapy will follow the schema outlined in the study protocol

PROGRESS

This study is designed for ER⁻ patients or ER unknown patients that do not fit into another category. Analysis shows an overall response rate of 57%; response rate to CT in ER unknown is 12/28 (43%) and in ER⁻ is 23/33 (70%). It is too early to comment on the value of Levamisole.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Advanced Carcinoma of the Breast with
Rubidazone.

WORK UNIT NO.: SWOG 7726

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy and toxicity of Rubidazone as determined by response rate and median duration of response in patients with disseminated carcinoma of the breast who have not received prior therapy with Adriamycin or other anthracycline antibiotics alone or in combination.

TECHNICAL APPROACH

Eligibility: All patients not eligible for higher priority Southwest Oncology Group studies with histologically proven advanced metastatic carcinoma of the breast who have not previously received Adriamycin or other anthracycline antibiotics. Patients must have a life expectancy of at least 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Ten patients of the 44 registered are not evaluable. The preliminary response rate, approximately 1%, appears inferior to Adriamycin.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemoimmunotherapy Utilizing BCNU, Hydroxyurea and DTIC with Levamisole vs. DTIC plus Actinomycin-D in the Treatment of Patients with Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7727

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine remission induction rates, remission duration, survival and toxicity in patients with disseminated malignant melanoma treated with BCNU, Hydroxyurea and DTIC (BHD), BHD plus Levamisole, and intermittent single high dose DTIC plus Actinomycin D in a prospective, randomized clinical study.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven disseminated malignant melanoma who have not been previously treated with any of the protocol agents shall be eligible. Patients must have measurable disease and estimated survival of at least 2 months.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study is too early to evaluate, but so far there is good accrual. There is no difference in response rate as yet.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-diamminedichloroplatinum in Refractory Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7730

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of high intermittent doses of cis-diamminedichloroplatinum in patients with advanced malignant melanoma refractory to higher priority protocol(s).
2. To determine the nature and extent of toxicity of this agent with the use of IV hydration only or IV hydration and mannitol diuresis.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed diagnosis of malignant melanoma. Patients must have metastatic disease and measurable lesion(s) refractory to higher priority protocol(s) for malignant melanoma. Expected survival should be a minimum of 10 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Accrual in this study is good, with 25 evaluable patients in each arm. Definite activity of Cis-Platinum is shown. There is a median of 3 doses given on the Cis-Platinum alone arm of the study. There has been one CR reported in the entire study. Previously treated patients have had less response, and there is little severe toxicity seen.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Anguidine in Advanced Soft Tissue and Bony Sarcoma.

WORK UNIT NO.: SWOG 7731

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the level of efficacy of the drug anguidine as a single agent in the treatment of advanced soft tissue and bony sarcomas in patients who have failed to respond or have relapsed on higher priority therapeutic regimens.
2. To determine the toxicity of anguidine in a Phase II trial.

TECHNICAL APPROACH

Eligibility: The patient must have a diagnosis of soft tissue or bony sarcoma confirmed by pathologic examination of tissue and must demonstrate either primary or recurrent disease which is not amenable to control with surgery, radiotherapy, or higher priority chemotherapy. Patient must have a project life expectancy of at least 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

There are 17 evaluable patients on this study. Thirteen have shown progressive disease, and four have shown stable disease. This drug is negative in sarcomas.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: CMF with or without Tamoxifen in Patients with Estrogen Receptor Positive Breast Cancer, Phase III Study.

WORK UNIT NO.: SWOG 7732

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine if the antiestrogen, Tamoxifen in combination with Cytosan, Methotrexate and 5-FU will alter the response rate, duration of response and median survival seen with Cytosan, Methotrexate and 5-FU alone in advanced human breast cancer, in patients who are estrogen receptor positive.

TECHNICAL APPROACH

Eligibility: Histological proof of recurrent breast cancer which is progressing. Measurable disease. Estimated survival greater than 10 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Due to poor patient accrual and publication of similar studies, this protocol was closed.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Rubidazone in Relapsing Lymphoma Patients Previously Untreated with Anthracycline Derivatives.

WORK UNIT NO.: SWOG 7734

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy, in terms of response rate, duration of response and survival, of the anthracycline antibiotic rubidazone in previously treated patients with Hodgkin's or non-Hodgkin's lymphoma.
2. To determine the maximum tolerated single dose in lymphoma patients.
3. To determine the critical cumulative cardiotoxic dose of rubidazone.

TECHNICAL APPROACH

Eligibility: Patients with histological diagnosis of Hodgkin's disease or non-Hodgkin's lymphoma who are not eligible for higher priority SWOG studies and who have had no prior anthracycline derivatives. Patients must have expected survival of 6 weeks or more.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study has poor patient accrual. If accrual does not improve, the study will be closed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Anguidine in Advanced Gastrointestinal Malignancies.

WORK UNIT NO.: SWOG 7735

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of anguidine and survival in terms of response rate and median duration of response, in the treatment of advanced gastrointestinal malignancies.
2. To observe any factors predisposing to excessive myelosuppression and for other toxicities not observed during Phase I studies of this drug.

TECHNICAL APPROACH

Eligibility: All patients with histologically proven gastrointestinal malignancies coming off studies with higher priority. Patients must have surgically incurable disease and objectively measurable parameters.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

In colon carcinoma, 18 patients are evaluable with only 1 PR; only 2 patients with no previous chemotherapy have been registered.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Anguidine in the Treatment of Urological Malignancies.

WORK UNIT NO.: SWOG 7736

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of anguidine in treating the major urological malignancies in terms of response rate, duration of responses, and survival.
2. To more fully study the adverse effects of anguidine and factors important in producing such effects.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven advanced urological malignancies (bladder, prostate, testis, renal pelvis, renal cell carcinoma). Life expectancy of at least 6 weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study was closed due to low patient accrual.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy of Pancreatic Adenocarcinoma with Mitomycin-C, 5-Fluorouracil and Streptozotocin.

WORK UNIT NO.: SWOG 7738

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine and document the response rates and toxicities of Mitomycin-C, Streptozotocin, and 5-FU compared to Mitomycin-C and 5-FU in the management of disseminated pancreatic adenocarcinoma.

TECHNICAL APPROACH

Eligibility: Patients with measurable and nonmeasurable disease will be eligible for this study. Patients with distant metastases (liver, peritoneum, etc.) and/or those in whom extension of the disease is outside of a port size greater than 15 x 15 cm.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Forty-five patients have been registered in each of the two treatment arms. There have been responses reported in both arms.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Pancreatic Carcinoma with Streptozotocin + 5-FU
+ Mitomycin-C, Phase I-II Pilot

WORK UNIT NO.: SWOG 7771

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the effectiveness as determined by response rate and survival of intra-arterial streptozotocin and systemic 5-FU and mitomycin-C in the treatment of adenocarcinoma of the pancreas with or without liver metastases localized to distribution of the celiac artery.
2. To determine the toxic effects resulting from such a combination.

TECHNICAL APPROACH

Eligibility: All patients must have a biopsy proven adenocarcinoma of the pancreas with the tumor confined to the distribution of the celiac artery (involvement of pancreas and liver only).

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Due to extremely slow patient accrual, this study was closed.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Pilot Study, Combined Chemotherapy for Advanced
Gastrointestinal Malignancies.

WORK UNIT NO.: SWOG 7801

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To determine the antitumor effect of anguidine as measured by response rate and survival, in combination with 5-FU in patients with advanced gastrointestinal malignancies.

TECHNICAL APPROACH

Eligibility: Only patients with histologically proven adenocarcinoma arising in the liver, gallbladder, biliary tree, exocrine pancreas, stomach, small intestines, colon and rectum are eligible. Patients must not have had prior exposure to fluoronated pyrimidines or anguidine.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

The protocol was designed for both good and poor risk patients. At present, the data indicate that patients with decreased myelosuppression also suffer decreased responses to treatment.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adjuvant Therapy of Soft Tissue Sarcomas with Radiation Therapy
+ Combination Chemotherapy.

WORK UNIT NO.: SWOG 7802

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether combination chemotherapy with A-DIC can improve the results in terms of disease-free survival produced by adjuvant radiotherapy in patients with soft tissue sarcomas Stage IIB and III at high risk for recurrent disease.
2. To determine any difference in toxicity between patients receiving boost radiation therapy to the scar from Cobalt 60 or electron beam.
3. To determine any difference in local recurrence rate or disease-free survival between patients with adequate surgery and those without adequate surgery.

TECHNICAL APPROACH

Eligibility: Patients with biopsy confirmed diagnosis of soft tissue sarcoma with Stage IIB or III who have undergone complete conservative surgical resection of the primary tumor and have no evidence of disease are eligible for this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Patient accrual has been extremely slow. If this does not improve the study will be closed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Baker's Antifol in the Treatment of Metastatic Renal Cell Carcinoma.

WORK UNIT NO.: SWOG 7803

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy of Baker's antifol in the treatment of metastatic renal cell carcinoma.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed metastatic renal cell carcinoma not eligible for studies of higher priority. All patients must have clearly measurable lesions with those being defined on liver scan being acceptable.

The major objective of this protocol is to determine if Baker's antifol is effective in at least 20% of patients with metastatic renal carcinoma. A total of 14 patients will be needed to evaluate this with an error of 5%.

PROGRESS

In six evaluable patients, no responses were seen. Therefore, the study was closed.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adjuvant Chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) vs. Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma.

WORK UNIT NO.: SWOG 7804

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the efficacy of adjuvant chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

TECHNICAL APPROACH

Eligibility: Localized lesions at least extending into the submucosa and involving any of the deeper layers with the maximum allowable penetration into but not through the serosa; localized lesions extending through serosa, with or without direct extension to continuous structures; a lesion diffusely involving the wall of the stomach with or without metastases to immediately adjacent perigastric nodes, or a localized lesion of any depth with metastases to perigastric nodes in the immediate vicinity; a localized or diffuse lesion with metastases to perigastric nodes distant from primary.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Nineteen patients have been registered. It is too early to analyze present data.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Medroxyprogesterone Acetate (MPA) Plus Yoshi 864 in Adult
Patients with Adenocarcinoma of the Kidney.

WORK UNIT NO.: SWOG 7805

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To determine the response rate and survival of patients with metastatic adenocarcinoma of the kidney to combined therapy with Yoshi 864 and Medroxyprogesterone Acetate (MPA).

TECHNICAL APPROACH

Eligibility: Only patients who have recurrent or metastatic adenocarcinoma of the kidney will be acceptable. Objectively measurable disease is required.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum in Refractory Epidermoid Carcinomas of the Esophagus.

WORK UNIT NO.: SWOG 7806

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

The purpose of this study is to determine the response rate and survival, with some degree of precision, utilizing cis-diamminodichloroplatinum II (CACP) in the treatment of patients with squamous cell carcinoma of the esophagus which is growing despite more standard therapy.

TECHNICAL APPROACH

Eligibility: Patients must have a biopsy-confirmed diagnosis of epidermoid carcinoma of the esophagus.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study has had three objective remissions; exact denominator is not clear. It is felt that cis-platinum plus radiotherapy would be the next step.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum in Refractory Epidermoid Carcinoma of the Lung.

WORK UNIT NO.: SWOG 7807

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To determine the response rate and survival in patients with epidermoid carcinomas of the lung who have demonstrated refractoriness to previous therapy utilizing Cis-Diamminodichloroplatinum.

TECHNICAL APPROACH

Eligibility: Patients must have epidermoid carcinoma of the lung confirmed, preferably by biopsy, although positive cytology is acceptable. Measurable disease is a requirement of this study.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Only one patient is evaluable with stable disease. It is too early for meaningful analysis.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Modality Treatment for Stage III and IV Hodgkin's Disease MOPP #6.

WORK UNIT NO.: SWOG 7808

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To attempt to increase the complete remission rate induced with MOP-BAP alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving a PR at the end of 6 cycles of MOP-BAP.
2. To determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when CR has been induced with 6 cycles of MOP-BAP in Stages III and IV Hodgkin's disease.

TECHNICAL APPROACH

Eligibility: The patient must have a histological diagnosis of Hodgkin's which must be classified by the Lukes and Butler system.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Seventeen patients have been entered and prestudy forms are available on 10 patients. Of the 5 patients on study long enough for a preliminary response evaluation, there is 1 CR, 3 PR's and 1 improvement.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Maytansine Therapy of Advanced Breast Cancer.

WORK UNIT NO.: SWOG 7809

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

To evaluate the effectiveness of Maytansine in terms of response rate and survival in patients with breast cancer resistant to standard therapeutic modalities.

TECHNICAL APPROACH

Eligibility: All patients will have histologically proven breast cancer resistant to known effective agents and not eligible for higher priority Southwest Oncology Group protocols. They should have an expected survival of six weeks.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

A total of 25 patients have been registered on this study. However, it is too early for analysis of results.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Brain Metastases Protocol.

WORK UNIT NO.: SWOG 7811

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the effectiveness of combined radiation therapy and metronidazole (Flagyl) in the treatment of patients with brain metastases from primary malignancies outside the central nervous system, compared with radiation therapy alone, as determined by objective response (brain and/or CAT scan) and/or increase in functional neurologic level and duration of response.
2. To determine the toxicity of multiple dose administration of metronidazole and radiation therapy.

TECHNICAL APPROACH

Eligibility: Patients must have histologic proof of a primary malignancy. There must be clinical suspicion of brain metastases documented by isotope brain scan and/or CAT scan. Patients must either have measurable disease on brain/CAT scan and/or neurologic status level of 2-4. Patients must have an expected survival time of at least one month.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Thirteen patients have been entered on this study. Four of four evaluable patients have shown partial response. Toxicity with Flagyl has been minimal.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Anguidine in CNS Tumors.

WORK UNIT NO.: SWOG 7812

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the antitumor activity of anguidine in the treatment of malignant gliomas relative to clinical response and survival.
2. To observe for expected and unexpected adverse effects and for factors important in producing these effects.
3. To determine the antitumor activity of anguidine in the treatment of malignant brain tumors in children and adolescents relative to clinical response and survival.

TECHNICAL APPROACH

Eligibility: Patients with histologically confirmed primary central nervous system tumors of the following histological types are eligible: Astrocytoma, grade III and IV; ependymoma; oligodendroglioma; and medulloblastoma. Patients under 21 years of age with a clinical diagnosis of recurrent brain stem glioma following radiation therapy will also be eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Patient accrual on this study has been poor. Of those eligible entries, it is too early to assess the results.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Methotrexate and Cis-Platinum for Patients with
Advanced Squamous Cell Carcinoma of the Head and Neck Region.

WORK UNIT NO.: SWOG 7814

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To determine whether Cis-Platinum will give a superior response rate
and/or a longer remission duration than Methotrexate in patients with
squamous cell carcinoma of the head and neck region.

TECHNICAL APPROACH

Eligibility: Patients who have histologically proven advanced squamous
cell carcinoma of the head and neck region which is not amenable to other
forms of therapy and who have measurable tumor lesions are eligible. It
is considered that all patients meeting these requirements have advanced
disease.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Some renal toxicity has been seen, and there has been difficulty in
collecting data for creatinine clearance. Patient accrual has been
slow.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Advanced Germ Cell Neoplasms of the Testis: Remission Induction with Vinblastine, Bleomycin, with Low-Dose or High-Dose Cis-Platinum; Surgical Removal of all Residual Tumor Following Remission Induction Maintenance Therapy with Cytosan, Actinomycin-D, Adriamycin and Vinblastine.

WORK UNIT NO.: SWOG 7817

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine in a randomized fashion the effectiveness of cis-diamine-dichloroplatinum (DDP) given in the conventional low-dose schedule daily x 5 days versus high-dose intermittent treatment in remission induction of disseminated testicular cancer, when combined with vinblastine and bleomycin.
2. To determine the survival of patients who achieve a partial remission and are rendered disease-free by surgical removal of residual disease and maintained on the same chemotherapy as patients who achieved complete remission status on chemotherapy alone.
3. To determine the effectiveness of cyclophosphamide, actinomycin-D, Adriamycin and vinblastine in the maintenance of remission status.
4. To document the nature and extent of the hematologic and nonhematologic side effects of the various drug combinations.

TECHNICAL APPROACH

Eligibility: All patients with metastatic testicular cancer of germinal cell origin regardless of prior radiation therapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Patient accrual has been slow. It is too early to evaluate results of therapy in the 14 patients entered on this study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Maytansine in Advanced Sarcoma, Phase II.

WORK UNIT NO.: SWOG 7820

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the antitumor effect as measured by response rate and median duration of response of maytansine against sarcoma.
2. To determine the nature of the toxicity of maytansine administered on a weekly dosage schedule.

TECHNICAL APPROACH

Eligibility: Patients should have biopsy proven incurable sarcoma and must not be eligible for any other protocol of higher priority. Patients must have measurable disease and an expected survival of at least six weeks.

Twenty-five patients will be entered into this study, which will permit estimation of the response rate with a standard error not greater than 0.10.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

There is good accrual on this study so far, and the drug is being well tolerated. However, it is still too early to evaluate the study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Maytansine in the Treatment of Relapsing Hodgkin's and Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 7821

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the antitumor effect of maytansine against advanced Hodgkin's and non-Hodgkin's lymphoma.
2. To determine the nature and extent of toxicity of maytansine administered on a weekly basis.

TECHNICAL APPROACH

Eligibility: Patients should have biopsy proven Hodgkin's disease or non-Hodgkin's disease, and must not be eligible for a higher priority protocol. Patients must have clearly measurable disease and an expected survival of at least 6 weeks.

Terhapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: ROAP-AdOAP in Acute Leukemia.

WORK UNIT NO.: SWOG 7823/24/25/26

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To compare the efficacy of the 4-drug combination chemotherapy regimen, ROAP (Rubidazone, Vincristine, Arabinosyl Cytosine, and Prednisone) to AdOAP (the same combination using Adriamycin in place of Rubidazone) in adult acute leukemia, as determined by remission rate, remission duration and survival.
2. To determine the comparative toxicity of these regimens.
3. To determine whether late intensification therapy at 9 months after complete remission will improve long-term, disease-free survival.
4. To determine whether immunotherapy using levamisole for 6 months after 12 months of complete remission on chemotherapy improves disease-free survival.
5. To determine reproducibility of the FAB/histologic classification and correlation to response to therapy in 200 consecutive cases of acute leukemia.
6. To determine the effects of intrathecal Ara-C on the incidence of CNS leukemia.
7. To study the effects of intensive supportive care in the management of acute leukemia.

TECHNICAL APPROACH

Eligibility: All patients over age 15 with a diagnosis of acute leukemia who have not received extensive therapy (defined as more than one course of any other chemotherapeutic agent or combination of agents)

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SWOG 7823/24/25/26 (Continued)

will be eligible for this study. The diagnosis of acute leukemia will be made on bone marrow smear, clot section and/or biopsy. An absolute infiltrate of 50% leukemic cells or greater is required.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Ninety-four patients have been entered on this study; however, only 14 are fully evaluable (FE) or partially evaluable (PE). Of the 14 patients that are FE or PE, 9 have been entered on AdOAP, 2 patients are classified as complete remission, 1 no response, and 6 patients are not classified with respect to response. Among the 5 patients entered on ROAP, 1 patient is classified as complete response, 1 no response and 3 are not classified by response.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Modality Therapy for Extensive Small-Cell Carcinoma of the Lung.

WORK UNIT NO.: SWOG 7828

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To improve the complete response rate and long-term, disease-free survival of patients with extensive small-cell carcinoma of the lung.
2. To define, quantitate and quantify the toxicity of each regimen employed.

TECHNICAL APPROACH

Eligibility: There must be a diagnosis by the institutional pathologist of small-cell, undifferentiated carcinoma of the lung. Extensive small-cell carcinoma includes the following: 1) Any patient with evidence of metastatic spread beyond the hemithorax and supraclavicular nodes on either side; 2) Any patient with a cytology-positive pleural effusion; and 3) Any patient with prior radiation therapy to the primary tumor, who presents with evidence of recurrent disease.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Carcinoembryonic Antigen as an Indicator for Second Look Surgery in Colorectal Cancer, A Randomized, Prospective Trial, Phase III.

WORK UNIT NO.: SWOG 7830

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether serial carcinoembryonic antigen (CEA) assays, following curative surgery, for Duke's B and C colorectal cancer leads to earlier detection of recurrence than standard follow-up procedures.
2. To determine whether recurrence detected through elevated CEA values, plus "standard clinical follow-up", leads to an improvement in the percentage of patients converted to no evidence of disease status following a second look surgery as opposed to recurrence detected by "standard" clinical means alone.
3. To determine whether there is a difference in crude survival between the CEA follow-up group and the standard follow-up group.

TECHNICAL APPROACH

Eligibility: The patient must have a completely resected Duke's B or C adenocarcinoma of the colon or rectum. Careful attention should be given to the examination of the liver. Suspicious areas should be biopsied to rule out metastatic disease. CEA values at 30 days post-initial resection must be normal; i.e., nonsmokers < 2.5 ng/ml, smokers < 5.0 ng/ml. Patients may be entered on the basis of institutional CEAs done 4-6 weeks post-op with normal defined above.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Chlorozotocin in Lung Cancer.

WORK UNIT NO.: SWOG 7832

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether chlorozotocin has significant activity as determined by response rate and median duration of response, against small-cell, large-cell, adenocarcinoma or squamous carcinoma of the lung.
2. To observe for toxicities of chlorozotocin not yet described and better define the known toxicities.
3. To determine factors predisposing to excessive toxicity of this agent.

TECHNICAL APPROACH

Eligibility: Patient must have histologically proven lung cancer and must have measurable lesions. Patient must be off all prior anticancer treatment for at least three weeks and recovered from all acute toxicities of prior treatment.

The anticipated accrual rate to this study is 8-10 eligible patients/month. At this rate it would be feasible to accrue the necessary 120 response-evaluable patients allowing for an overall inevaluability rate of 20-25%.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Six patients have been registered thus far; however, it is too early for evaluation of results of therapy.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chlorozotocin in Gastrointestinal Cancer.

WORK UNIT NO.: SWOG 7833

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether chlorozotocin has significant activity as determined by response rate and median duration of response, against colon, pancreatic, hepatic and gastric adenocarcinoma.
2. To observe for toxicities of chlorozotocin not yet described and better define known toxicities.
3. To determine factors predisposing to excessive toxicity of this agent.

TECHNICAL APPROACH

Eligibility: The patient must have histologically proven gastrointestinal cancer which is unresponsive to standard forms of treatment or for which standard treatments have proven of little or no value.

In order to estimate the response rate in colon patients with a standard error not greater than $\pm 10\%$, at least 25 response-evaluable patients must be accrued.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: High Dose Vincristine, Prednisone, Hydroxyurea and Cytosine Arabinoside (HOAP) in the Blastic Phase of Chronic Granulocytic Leukemia, Phase III.

WORK UNIT NO.: SWOG 7835

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard a. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the effectiveness as determined by remission rate, on the combination of high-dose vincristine, prednisone, hydroxyurea, and cytosine arabinoside (HOAP) for remission induction in patients with the blastic phase of chronic granulocytic leukemia.
2. To compare the effectiveness of this regimen in myeloid versus lymphoid blastic transformation, and in patients with poor prognostic characteristics, namely hyperdiploidy and lack of terminal deoxynucleotidyl transferase (TdT).
3. To evaluate the value as determined by median duration of remission and survival, of an intensive intermittent regimen of cytosine arabinoside, prednisone, and vincristine in the maintenance of remission.

TECHNICAL APPROACH

Eligibility: All patients with chronic granulocytic leukemia in whom a diagnosis of blastic crisis has been made, and who exhibit all of the following criteria: 1) increasing leukocyte count with or without progressive anemia and/or thrombocytopenia, resistant to conventional drugs used in the chronic phase of the disease; 2) more than 25% blasts, plus granulocytes in the bone marrow and/or peripheral blood; 3) progressive enlargement of the spleen in nonsplenectomized patients.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy for Metastatic Epidermal Carcinoma of the Anal Canal, Phase II.

WORK UNIT NO.: SWOG 7836

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the antitumor effect of bleomycin, Adriamycin, mitomycin-C, and 5-FU as measured by response rate and survival in epidermal carcinoma of the anal canal.
2. To use the patient accrual capabilities of the Southwest Oncology Group to gather sufficient patients in this relatively uncommon tumor to arrive at a statistically valid response rate.

TECHNICAL APPROACH

Eligibility: All patients must have histologically proven metastatic squamous cell carcinoma of the anal canal or metastatic cloacogenic carcinoma.

In order to estimate the overall response rate with a standard error of not greater than $\pm 10\%$, at least 25 response-evaluable patients must be accrued.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This study was recently activated, and it is too early for a report.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II-III Comparison of FAM vs. FAM + Vincristine vs. Chlorozotocin in the Treatment of Advanced Gastric Adenocarcinoma.

WORK UNIT NO.: SWOG 7841

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine whether or not vincristine increases the effectiveness (as determined by response rate and survival) of 5-FU plus mitomycin-C plus Adriamycin (FAM) in the treatment of advanced, previously untreated gastric adenocarcinoma.
2. To determine the efficacy as determined by response rate and survival of chlorozotocin in the treatment of previously untreated gastric adenocarcinoma.
3. To determine by crossover, after relapse or failure on FAM, V-FAM or chlorozotocin, the effectiveness, as determined by response rate and survival, of the alternate treatment in advanced gastric adenocarcinoma with prior therapy.
4. To determine the toxicities of such treatments.

TECHNICAL APPROACH

Eligibility: Patients must have histologically proven gastric adenocarcinoma, Stage IV in extent to be eligible. They must not have received prior chemotherapy nor should they have received radiotherapy within 4 weeks of entry. Patients must have a minimum life expectancy of 6 weeks and a performance status of 0-3 in order to be eligible.

The Phase II evaluation of chlorozotocin will require entry of 35 eligible patients. The Phase III comparison of FAM vs. V-FAM will attempt to detect a 25% increase in response rate on the latter arm.

SWOG 7841 (Continued)

PROGRESS

This is a new study, and it is too early for a report.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combined Therapy with Celiac Artery Infusion 5-FU Plus Radiation Therapy Followed by Mitomycin-C and 5-FU Maintenance Chemotherapy for Treatment of Localized Adenocarcinoma of the Exocrine Pancreas.

WORK UNIT NO.: SWOG 7861

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the effect on survival in localized pancreatic cancer by utilizing direct celiac artery infusion of 5-FU combined with radiation therapy and Mitomycin, 5-FU maintenance therapy.
2. To establish the toxicities of this multimodality in a pilot study and test feasibility for widespread cooperative group use.

TECHNICAL APPROACH

Eligibility: Histological confirmation of adenocarcinoma of the exocrine pancreas. Tumor margin as outlined by radiopaque clips to create a port size not greater than 225 cm² (approximately 15x15 cm). Alternately, patients are eligible if a similar port can be constructed based on arteriographic findings or with ultrasonography. Patients with local extension of disease into stomach, vertebral body, liver or lymph node are eligible for this study as long as the field size meets the stated criteria.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Of the seven evaluable patients, all patients have experienced minimal to no toxicity during the initial phase of the treatment program. The data obtained on these seven patients indicate that the induction program is a safe and acceptable treatment modality for use in the Phase III study. There have been some problems encountered in the maintenance phase of severe hematologic toxicity primarily related to the initial dose of Mitomycin-C. Therefore, the protocol is amended to lower the

SWOG 7861 (Continued)

dose of Mitomycin-C in the maintenance phase from 15 mg/m^2 to 10 mg/m^2
IV q 8 weeks.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Concurrent CT-RT of Selected Head and Neck Cancer.

WORK UNIT NO.: SWOG 7863

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To assess the local and systemic toxicity of the concurrent administration of the chemotherapeutic agents, bleomycin and hydroxyurea, with super voltage radiotherapy in the treatment of locally advanced squamous cancer of the head and neck.
2. To determine the maximum tolerated dose of both chemo-and radiotherapy when given according to the proposed regimen.

TECHNICAL APPROACH

Eligibility: Patients with locally advanced (T₂ or T₄) squamous cell carcinoma of the head and neck who are candidates for definitive or palliative radiotherapy are eligible. Patients must have histologic confirmation of their disease and must have measurable disease.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

Patient accession has been low with only 10 patients registered.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Advanced (Stages III and IV) Hodgkin's Disease: Remission Induction with CHOP: Groupwide Study for MOPP Failures without Prior Anthracyclines, Phase II.

WORK UNIT NO.: SWOG 7903

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the effectiveness, as determined by response rate, of the CHOP combination of chemotherapy for remission induction in patients with advanced (Stages III or IV) Hodgkin's disease who have not had prior chemotherapy and in those with prior MOPP (no anthracyclines).
2. To assess the length of unmaintained remissions after intensive induction with ten courses of treatment with CHOP and after documentation of CR by restaging.
3. To evaluate the degree of noncross-resistance of CHOP in MOPP failures in terms of remission induction, duration of remission and survival.
4. To compare the toxicities and side effects of the CHOP regimen to those of MOPP.

TECHNICAL APPROACH

Eligibility: Patients must have histologic diagnosis of Hodgkin's disease classified by the Lukes & Butler System in order to be eligible. They must have stage of disease classified by Ann Arbor staging criteria and must be clinical or pathological Stages III or IV if previously untreated. Relapsing patients may have any extent of disease; however, staging procedures sufficient to gauge response are required.

Therapy will follow the schema outlined in the study protocol.

SWOG 7903 (Continued)

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hexamethylmelamine vs. FAC in Advanced Transitional Cell
Bladder Carcinoma in Patients with Impaired Renal Function,
Phase II-III.

WORK UNIT NO.: SWOG 7904

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To compare the efficacy (response rate) of hexamethylmelamine versus
FAC (5-Fluorouracil, Adriamycin and Cyclophosphamide) in locally re-
current or disseminated transitional cell bladder carcinoma, in
patients with impaired renal function, with crossover upon treatment
failure.

TECHNICAL APPROACH

Eligibility: Patients with histologically proven T₄ transitional cell
bladder carcinoma, if there is a contraindication to radical surgery
or radiotherapy, and recurrent or residual cases after surgery, radio-
therapy or both; and M₁ cases with liver, osseous, pulmonary or other
metastases are eligible.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: VP-16-213 in Acute Monocytic and Myelomonocytic Leukemias,
Phase II.

WORK UNIT NO.: SWOG 7907

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the effectiveness of VP-16 in the induction of remission in acute monocytic leukemia and myelomonocytic leukemia in relapse.
3. To evaluate remission maintenance with VP-16.

TECHNICAL APPROACH

Eligibility: Patients of all ages with the diagnosis criteria of acute monocytic leukemia or acute myelomonocytic leukemia in relapse after previous treatment are eligible, provided that VP-16 has not been given to them previously. Cytomorphology must conform with the diagnosis of acute myelomonocytic leukemia or acute monocytic leukemia.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Vinblastine Sulfate in the Management of Resistant Chronic
Myelogenous Leukemia, Phase II.

WORK UNIT NO.: SWOG 7908

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

To determine the incidence, quality and duration of responses to
vinblastine sulfate among previously treated patients with chronic
myelogenous leukemia.

TECHNICAL APPROACH

Eligibility: Chronic myelogenous leukemia patients previously treated
with radiation therapy and/or alkylating agent (single or combination)
and failing due to drug resistance are eligible. Patients must have
progressive disease, and must be off previous chemotherapy.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Estrogen-Antagonist in the Management of
Refractory Large Bowel Tumors, Phase II.

WORK UNIT NO.: SWOG 7910

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.S., MAJ, MC

OBJECTIVES

To help judge whether there is any therapeutic significance in humans to the laboratory observation that some colorectal tumors, in men and women, have estrogen receptors; as determined by response rate to tamoxifen.

TECHNICAL APPROACH

Eligibility: Patients must have biopsy confirmed diagnosis of adenocarcinoma of the large bowel.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Evaluation of Gallium Nitrate in Soft Tissue and Bone Sarcomas.

WORK UNIT NO.: SWOG 7911

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy of gallium nitrate in patients with soft tissue and bone sarcomas, who have failed on higher priority treatment protocols.
2. To determine the nature and degree of toxicity of this drug.

TECHNICAL APPROACH

Eligibility: All patients not eligible for higher priority studies with histologically proven incurable advanced soft tissue and bone sarcomas are eligible. Patients must have a life expectancy of at least 6 weeks and must have clearly measurable disease.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Gallium Nitrate in Patients with Malignant Lymphoma -
Hodgkin's and non-Hodgkin's, Phase II.

WORK UNIT NO.: SWOG 7912

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S.
Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the efficacy, as measured by response rate, of gallium nitrate in patients with malignant lymphoma, both Hodgkin's and non-Hodgkin's types, in patients who have received prior therapy and are not eligible for higher priority studies.
2. To determine the nature and degree of toxicity of this drug.

TECHNICAL APPROACH

Eligibility: All patients with malignant lymphoma who are not eligible for higher priority protocols are eligible. Patients must have a life expectancy of at least 6 weeks and clearly demonstrable disease.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Colchicine in Refractory Hodgkin's Disease, CLL, Lung and Breast Cancer.

WORK UNIT NO.: SWOG 7960

PRINCIPAL INVESTIGATOR: J. Dean McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Richard A. Shildt, M.D., MAJ, MC; Merrill S. Kies, M.D., MAJ, MC

OBJECTIVES

1. To determine the maximum dose of colchicine which may be safely administered on a once weekly basis.
2. To determine the response rate (standard error \pm 10%) to weekly, intravenous colchicine in each of the tumor types tested.
3. To determine quantitative and qualitative toxicity of the drug on this schedule.

TECHNICAL APPROACH

Eligibility: Patients with chronic lymphocytic leukemia, Hodgkin's disease, breast and lung cancer (both small and nonsmall cell) are potential candidates after they have developed progressive disease on SWOG protocols of higher priority. They must have a life expectancy of at least 6 weeks and a Performance Status of 0-3. Measurable disease is desirable but not required.

It is estimated that 30 patients in each category will need to be entered in order to have 25 patients which are response-evaluable.

Therapy will follow the schema outlined in the study protocol.

PROGRESS

This is a new study.

Status: Ongoing.

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